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The major purpose of this 4-year study was to determine the effects of the Comprehensive Coping Strategy Program (CCSP) on pain, fatigue, psychological distress, nausea, health status, burden of care and quality of life in breast cancer patients and their primary caregivers. A randomized controlled clinical trial design was used. 138 patients and 102 primary caregivers participated in the study. Seventy patients were randomly assigned to the CCSP treatment group and 68 to the control group. Data were collected 20 days before hospitalization (baseline), during hospitalization (7 days after the ABMT), and again during the post hospitalization period which was ≥ one year following the ABMT. The results showed that breast cancer patients experienced pain, fatigue, nausea and psychological distress prior to, during and post-hospitalization for ABMT. Depression, pain, fatigue and negative coping (catastrophizing) accounted for 41% to 65% of the variance in health status. The CCSP treated group of patients experienced less nausea ($p<.01$), less fatigue and nausea ($p<.05$), 8.5 times less likely to die ($p=.05$), and a higher quality of life ($p<.05$ to $p<.01$) than patients in the control group. Preliminary results related to the patients' primary caregiver at baseline show that they suffer from moderate anxiety. Anxiety and fatigue were more severe in females and PCGs who were single ($p<0.05$ to $p<0.01$). Family, a subscale of quality of life, was predictive of burden of care (Beta= -2.45, $p<0.05$). Follow-up data for PCGs will be analyzed during the final year of the study.

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Tammie Gaston-Johnson

PI - Signature Date

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I. Introduction

Autologous bone marrow transplantation (ABMT) consists of the administration of high-dose chemotherapy and in some cases, total body radiation, followed by rescue with autologous, cryopreserved, bone marrow cells. This treatment regimen has become an established alternative treatment in a variety of malignant diseases including breast cancer[1]. While potentially life-saving, ABMT can be a traumatic procedure and can seriously impact the patient's quality of life (QOL). The often severe and unrelenting pain from the treatment regimen, medical procedures and persistent adverse physical side effects such as pain, fatigue and nausea and vomiting result in a critically ill and psychologically distressed patient. These symptoms in turn affect the patient's health status and QOL[2-3]. The patient's primary caregiver may also experience psychological distress, severe fatigue, increased burden of care, and a less than optimum QOL[4-9].

The overall purpose of this study was to measure the effects of a comprehensive coping strategy program (CCSP) on pain, psychological distress, fatigue, perceived health status, burden of care, and QOL for breast cancer ABMT patients and their primary caregivers.

II. Literature Review

A. ABMT Patients

Pain associated with ABMT is well documented and is related to either the conditioning regimen and/or the ABMT procedure itself. Painful side effects of ABMT include the following: gastrointestinal complications- painful effects on the epithelial membranes of the oral cavity (stomatitis and ulcerations); gastritis, diarrhea and nausea and vomiting; genitourinary complications- painful effects on the mucosal epithelial membranes of the bladder wall (chemical cystitis), renal complications; veno-occlusive disease; pancytopenia effects- infection, high fever, sepsis, hemorrhage; neurological complications; cardiac toxicities; alopecia with resultant effects on body image; and fatigue[2, 3, 10]. ABMT treatment causes pain through necessary invasive procedures such as bone marrow aspirations, spinal taps and Hickman Catheter placement. Rappaport[11] reported that anxiety and depression were the most common psychological reactions in patients post-ABMT. The subtle and overt interrelationships among the many potential physical and psychological symptoms related to ABMT make care of this population a very complex process.

As ABMT therapeutic advances for breast cancer have led to improvement in prognosis and overall survival, emphasis on the psychosocial well-being of the patient has become more important[12]. Anxiety regarding painful procedures, strict protective isolation, and depression were universal reactions during and for several months following ABMT[13]. Gaston-Johansson and associates[5] found that ABMT patients had moderate anxiety and depression during hospitalization and at discharge with anxiety and depression reaching peak intensity 5 days post ABMT. Jenkins and associates[14] found that 40% of ABMT patients, suffered from major depression at some stage during the transplant procedure. Case studies and anecdotal description suggest that strict protective isolation, medical procedures, and pain are frequent contributors to anxiety and depression in ABMT patients, with pain described as the most frequent factor[14]. Research documenting a positive relationship of pain to anxiety and depression in cancer patients is extensive[15, 16].

About 33-76% of patients who undergo ABMT experience a high degree of fatigue[17]. Frequency and severity of pain, psychological distress and fatigue influences a patient's perceived health status, QOL and length of hospital stay[18]. Additional research targeting treatment-related fatigue and patient response to this symptom

is needed[19].

Coping strategies of breast cancer patients have been recognized as a critical component of psychosocial well-being. Some of the psychological aspects of the BMT process are well-known: decreased contact with supportive persons because of protective isolation; anxiety related to the unpredictability of the progress through the BMT experience; and side effects[20]. Numerous factors affect psychosocial reactions to the BMT experience: age; social support; personality/intelligence; financial worries; religion; culture; and past experiences[21]. However, few longitudinal studies conducted over time to explore these factors have been completed[22]. Although few studies have been conducted to identify psychosocial aspects of the BMT experience from the patient's perspective, a hermeneutical inquiry was conducted which identified five major themes of coping patterns among BMT patients: physiological functioning; alertness; attitude; social relationships and; spirituality[20].

A patient's beliefs about his/her health status have been shown to be an important determinant of health outcomes[9]. The health status of ABMT patients varies. Some breast cancer ABMT patients leave the hospital within three weeks, while others stay 2 to 3 months. About 35% of patients utilize emergency room services and about 15 to 50% require one or more rehospitalizations[23].

B. Primary Caregiver (PCG)

It is well recognized that cancer impacts not only the patient, but also persons who comprise the patient's support system[24, 25, 26, 27, 28]. Northouse[28] presented summary empirical evidence from 19 studies that families may experience similar emotions as the breast cancer patient. The PCG is the person identified by the patient as the significant other. The PCG is usually the single greatest support person for the patient during the transplant process and at other difficult times[29]. Not only does the PCG devote energies to the patient during the pretransplant period and peritransplant period, but also because of the decreased length of stay for the ABMT patient additional responsibilities may be added: dispensing oral medications and administering intravenous fluids and medications via an infusion pump; and assessment of the patient in the home for sequel of the ABMT process- fever, nausea and vomiting, diarrhea or other reportable side effects and symptomatology[30]. Few studies to date have documented the PCG's psychological distress or negative outcomes related to care of the breast cancer ABMT patient, or how they cope with problems related to caregiving burden. Pistrang and Barker[26] explored the role of the helping relationship with the partner related to women's psychological response to breast cancer. Their findings suggest that the partner plays a key role in breast cancer patients' adaptation and also that interventions focusing on couples may be effective in reducing psychological distress[26]. Burdens which can contribute to this distress include the patient's medical regimen, the constant/multiple patient demands prior to, during and months/years after ABMT, possibly traveling long distances and displacement from home, friends and work, possibly living with a very ill person for a long time, and competing family/work responsibilities. There is some evidence that caregivers experience positive reactions[29]. However, most investigators suggest that caregivers responsibilities have negative effects on the caregivers' QOL[6]. Caregivers frequently demonstrate poor health and severe fatigue, in addition to frustration, anxiety and depression. Improving support within this close relationship may lessen PCG burden of care and allow for better adjustment to the cancer experience for both the patient and the PCG.

C. Comprehensive Coping Strategy Program (CCSP)

The Gate-Control Theory of pain by Melzack and Wall[15] and the Stress, Coping and Adaptation Paradigm by Lazarus[16] provide the theoretical framework for this study. Pain is defined as a multi-dimensional sensory and affective experience associated with discomfort[15]. Coping is defined as constantly changing cognitive

and behavioral efforts used to manage specific external and /or internal demands that are appraised as taxing or exceeding the resources of a person[16]. Positive coping strategies refer to internal thoughts and behaviors people use to manage their pain, or their emotional reactions to the pain and to reduce emotional distress. Catastrophizing, a negative coping strategy, is defined as a method of cognitive coping characterized by negative self-statements and thoughts about the future[23, 31].

Previous research studies have shown that pain and emotional distress can be reduced in pain patients by providing a comprehensive coping strategy program (CCSP) which includes: preparatory information to increase control[31]; b) cognitive restructuring which includes positive coping statements and avoidance of catastrophizing[31]; and c) relaxation with guided imagery. A combination of these three components has been found to be the best overall coping intervention to reduce pain and stress rather than using each component separately[31]. However, no prospective or retrospective study was found in the scientific literature which included these three components in a unified coping strategy program to reduce pain and emotional distress and fatigue in breast cancer ABMT patients.

III. Hypotheses

Hypotheses examined were:

A. Breast cancer patients who receive ABMT and participate in a CCSP will demonstrate greater improvements over time in pain, psychological distress, fatigue, perceived health status, and quality of life than breast cancer ABMT patients who do not receive the CCSP.

B. Primary caregivers, of breast cancer patients who receive ABMT and participate in a CCSP, will demonstrate greater improvement over time in burden of care, psychological distress, fatigue, and quality of life than primary caregivers of ABMT patients who do not receive the CCSP.

IV. Research Objectives

A. Research objectives Hypothesis A:

1. To describe pain, psychological distress, and health status in breast cancer patients during the pre-hospitalization for ABMT time period.
2. To examine the relationships among pain, psychological distress, catastrophizing, coping, and perceived health status in breast cancer patients during the pre-hospitalization for ABMT time period.
3. To describe the percentage of variance within the concept of health status which was explained by pain, psychological distress, and coping.
4. To describe the prevalence and severity of fatigue, pain, depression, and alterations in health status in breast cancer patients with metastatic disease.
5. To determine if fatigue, pain, and depression and catastrophizing are significant predictors of health status.
6. To determine if a significant difference existed in the pain, fatigue, psychological distress, and nausea between patients with breast cancer who receive ABMT and the CCSP and patients with breast cancer who receive ABMT but do not receive the CCSP.
7. To determine if a Comprehensive Coping Strategy Program has an effect on mortality and survival in breast cancer patients treated with ABMT.
8. To determine if patients with breast cancer find a comprehensive coping strategy program

beneficial.

9. To determine the effects of a comprehensive coping strategy program on quality of life in patients with breast cancer who have undergone an ABMT.

B. Research Objectives related to Hypothesis B

1. To describe psychological distress, fatigue, burden of care and quality of life in primary caregivers of patients who have been treated for breast cancer and are scheduled for ABMT.
2. To determine the effect of a comprehensive coping strategy program on psychological distress, fatigue and burden of care in primary caregivers of patients who undergo bone marrow transplant for breast cancer.

V. Methods and Instrumentation

A. Study Design

The study has a prospective randomized controlled clinical trial design with repeated treatment and measurements. Participants were randomized to one of two comparison groups for the purpose of measuring the effect of the proposed intervention, i.e. participation in the CCSP. Group I was composed of breast cancer patients and their PCGs who received the CCSP intervention. Group II included breast cancer patients and their PCGs who did not receive the CCSP. Eligibility criteria for participation in the project were as follows: 1) scheduled to receive ABMT for stage II, III or IV breast cancer; 2) able to speak and read English; 3) age> 18; 4) able to give informed consent.

B. Subjects: Participation Rate and Follow-up of Patients

The number of patients who entered the study were 142 of which 4 declined participation (Figure 1). The subjects were recruited to the study over a period of 31/2 years.

1. Baseline

At baseline, data were collected on 138 subjects. Following the collection of baseline data, 68 subjects are randomly assigned to a control group and 70 to the CCSP treatment group.

2. During Hospitalization

Of the 138 subjects on which baseline data were collected, only 110 subjects remained in the study when data were collected 2 days before and 7 days after the bone marrow transplant. Fifty-eight were in the control group and 52 in the CCSP treatment group. The number of subjects decreased because 10 were too ill to complete questionnaires, 8 had their ABMT canceled, 3 died and 7 withdrew from the study (Figure 1).

3. Post-Hospitalization Follow-up - ≥ to 12 Months

Of the 110 subjects on which data were collected during hospitalization, data were collected during post-hospitalization on 70 plus an additional 3 subjects who had completed baseline data, but were too ill to participate during hospitalization. Thirty-five subjects were in the control group and 38 in the CCSP treatment group. The number of subjects decreased because 13 of the 110 subjects died prior to follow-up, and 27 had not at the time of this report reached the time required for follow-up (Figure 1).

C. Subjects: Participation Rate and Follow-up of PCGs

The number of PCGs who participated in the study at baseline were 102 of which 55 were in the CCSP treated group and 47 PCGs in the control group. There were 72 PCGs remaining in the study during the patients hopitalization. Follow-up of the PCG ≥ 12 months remaining in the study after the patients ABMT is in progress.

D. Patient Variables and Instruments

1. Sociodemographic and Background Variables

The information about demographic and background variables was collected on a standardized form and included the following information: age; gender; race/ethnicity; marital status; educational level; religion; household income; employment status; occupation; and whether the subjects lived alone or with another person.

2. Pain Intensity and Quality

The Painometer(r) (POM) is a hard white plastic tool which measures 8 inches long, 2 inches wide and 1 inch thick. It is light weighted and can easily be held by the subject. A list of 15 sensory and 11 affective pain descriptors are located on the front side of the POM and a 100 mm visual analogue scale with a moveable marker is located on the back side of the POM (POM-VAS). An intensity value (from a low of one to a high of five) is pre-determined for each sensory and affective word located on front of the POM. A maximum score can be obtained for the sensory component of pain and for the affective component. A total score can be obtained by adding the sensory and affective scores. Test-retest reliability of the POM has been demonstrated as well as criterion related[34] and construct validity[32-36].

3. Psychological Distress

Anxiety and depression were assessed as measures of psychological distress. Anxiety was measured using the State-Trait Anxiety Inventory (STAI). The STAI consists of two separate self-report scales for measuring state and trait anxiety[37]. State anxiety is a transitory emotional response to a stressful situation. Trait anxiety reflects a stable predisposition to anxiety as determined by a personality pattern. Respondents rate themselves in relationship to the statement on a Likert scale from 1 to 4. The total score is the sum of all 20 responses and ranges from a minimum score of 20-39 (low anxiety), 40-59 (moderate anxiety), to a maximum score of 60-80 (high anxiety). Test-retest reliability and validity have been demonstrated for the STAI[37]. Depression was measured using the Beck Depression Inventory (BDI). The BDI consists of 21 items that describe particular symptoms of depression[38]. Subjects respond to a Likert-type scale by rating each item 0 (no symptom) to 3 (severe or persistent presence of the symptom). Scores ranging from 0 to 9 are normal, 10 to 15 mild depression, 16 to 23 moderate depression, and 24 to 63 severe depression. The total score (range 0 to 63) is obtained by summing the 21 responses. Test-retest correlations of the BDI ranged from .60 to .90 in nonpsychiatric patients[38].

4. Fatigue and Nausea

The Piper Fatigue Scale (PFS) was used to measure fatigue. This scale was designed to measure fatigue as a multidimensional phenomenon, defined as "a subjective feeling of tiredness, influenced by circadian rhythm, and other factors varying in duration, unpleasantness, and intensity"[39]. The scale consists of 41 horizontal 100

mm VAS items measuring four dimensions of subjective fatigue: 1) temporal dimension; 2) intensity/severity dimension; 3) affective dimension; and 4) sensory dimension. A total fatigue score is calculated by summing the four scores and dividing by four[39] . A 100 mm visual analogue scale was also used to measure overall fatigue and nausea.

5. Perceived Health Status

The Short-Form Health Survey (MOS-FS)[40] was used to measure perceived health status. The 20-item survey assesses physical functioning (6 items), role functioning (2 items), social functioning (1 item), mental health (5 items), health perception (5 items) and pain (1 item)[40]. Reliability[40] and construct validity has been demonstrated for the MOS-SF.

6. Coping Strategies

The Coping Strategy Questionnaire (CSQ), developed by Keefe[23], will be used to assess a person's use of pain coping strategies. The categories of coping strategies assessed by this measure include:1) diverting attention; 2) reinterpreting pain sensations; 3) ignoring pain sensations; 4) praying and hoping; 5) catastrophizing; and 6) increasing activity level. For each category of coping strategies there are 6 items on the CSQ with scores ranging from 0 to 36. Each item is rated on a 7 point scale to indicate how often that strategy is used to cope with pain (0 = never, 3 = sometimes, and 6 = always). The CSQ also includes 2 items which measure overall effectiveness of those strategies used by asking the subjects to rate on a 7-point scale (with scores ranging from 0 to 6) how much control they have over the pain, and how much they are able to decrease their pain23. Reliability and construct validity have been demonstrated for the CSQ[23].

7. Burden of Care

Burden of care (BOC) was assessed using the Measurement of Objective Burden (MOB) and the Measurement of Subjective Burden (MSB) scales developed by Montgomery, Gonyea and Hooyman41. The MOB is a 9-item, 5-point scale ranging from (1), " a lot more or better", to (5), "a lot less or worse", designed to assess the extent to which caregiving behaviors have changed the caregiver's lives in nine areas: time for oneself; privacy; money; personal freedom; energy; recreational/social activities; vocational activities; relationships with other family members; and health. The MSB is a 13-item, 5-point scale from (1) "rarely or never" to (5) "most of the time", designed to assess attitudes toward or emotional reactions to the caregiving experience. Items for the MSB were adapted from the 29-item inventory relating to attitudes and feelings about caregiving developed by Zarit and associates[42]. Reported alpha was .85 for the MOB scale and .86 for the MSB scale[41].

8. Quality of Life

QOL was measured by the Quality of Life Index (QLI), which consisted of 35 items that are categorized into the following subscales[43]: health and functioning, socioeconomic, psychological/spiritual, and family. The tool uses 6-point ordinal scales to measure both the satisfaction with and the importance placed on each item by the individual. Responses range from 1 (very dissatisfied/unimportant) to 6 (very satisfied/important). Final scores ranged from 0 to 30, with higher scores indicating greater QOL[43].

Reliability and validity of the QLI were established in a number of studies by Ferrans[43]. Concurrent validity was supported by a strong correlation (r = 0.80) between the QLI and a question evaluating overall staisfaction with life. Alpa reliability for the total score was 0.95. Internal consistency was reported for the subscales on

the QLI at 0.90 for health and functioning, 0.84 for socioeconomic, 0.93 for psychological/spiritual, and 0.66 for family[43].

E. CCSP Intervention

Purposes

The three purposes of the CCSP are to: 1) teach the patient and PCG how to decrease and control pain and discomfort; 2) enhance the coping ability of the patient and PCG by teaching them to recognize distorted thinking, and how to use positive coping self-statements and; 3) teach the patient and PCG how to use relaxation with imagery. The goal of the CCSP is to reduce pain, psychological distress, and reduce fatigue that is known to be intensified by pain and psychological distress. A decrease in these symptoms is expected to positively influence the subjects perceived health status and QOL. A detailed description of the CCSP is presented in the Appendix A.

F. Data Collection Procedure, Statistical Analysis and Results

Data collecting procedures, statistical analysis and results specific to each patient objective 1 - 7 are presented in Papers I - IV (See Appendix B-E). Work is in progress for the remaining objectives, however, results based on preliminary data analysis are presented in this document.

G. General Statistical Analysis

For each time periods of data collection: baseline, during hospitalization and post hospitalization, exploratory data analysis examining distribution, outliers and missing data were routinely performed prior to any bivariate association testing. No imputation or extrapolation was made for values which were missing or fell out of range. Number of subjects under these categories were extremely small however, and thus did not influence final results. The scores for all physiological (pain, fatigue) psychological(anxiety, depression, coping), QOL, health status domains were computed using the weighted number of items answered for a particular sub-scale by the respondent. However, the subject was omitted from that sub-scale if she had less than 50% of the items in a particular sub-scale reported. Additionally, the direction of the sub-scale scores were also reviewed in relation to standard range and direction of the score reported in the original instrument. Subsequent correlation coefficients, means and standard deviations, and independent association of proportions were obtained and compared between the treatment and control groups, to evaluate the significance of the association at cross-sectional and longitudinal levels. Finally, to test hypothesis originally proposed, multiple linear and logistic regressions were performed to determine the treatment effectiveness, when co-variates were taken into account.

VI. Results

A. A summary of findings related to Objectives 1-7 are presented below (Appendix B-E):

Gaston-Johansson, F., Fall-Dickson J., Bakos, A., Kennedy, J. (1998) Fatigue, Pain, and Depression as Predictors of Health Status in Breast Cancer Patients (The Role of Symptoms in Health Status) (Submitted to Cancer Nursing)

In **manuscript number 1**, our research team was able to characterize the multiple symptoms (fatigue, pain, depression) experienced by women with breast cancer who were treated with mastectomy and chemotherapy

prior to autotransplantation. We were also able to show that pain and depression accounted for 60% of the variance in total health status, and that fatigue and depression accounted for 41% of the variance in the patients perception of her health status. A patient's beliefs about his/her health status have been shown to be an important determinant of health outcomes.

Gaston-Johansson, F., Ohly, K., Fall-Dickson J., Nanda, J., Kennedy, J. (1998) Pain, Psychological Distress, Health Status, and Coping in Breast Cancer Patients scheduled for Autologus Bone Marrow Transplant (Submitted to Oncology Nursing Form).

In **manuscript number 2**, our research team was able to characterize pain, psychological distress, health status and coping experienced by women with breast cancer who were treated with mastectomy and chemotherapy prior to autotransplant We found that 24% of the patients suffered moderate anxiety and 26% suffered from severe\high anxiety. Moderate depression was experienced by 17% and severe\high depression was reported by 7% of the subjects. The subjects reported a mean total health status score of 50.30 (SD = 10.67, range 18 to 72) out of a possible score ranging from 0 to 91. There were strong correlations between depression and total health status (-.73,$p<0.001$). We also found that sensory pain, depression and catastrophizing (a negative coping strategy) accounted for 65% of the variance in health status.

Gaston-Johansson, F., Fall-Dickson J., Nanda, J., Ohly, K., Stillman, S., J., Kennedy, J. (1998) The Effectiveness of a Comprehensive Coping Strategy Program on Clinical Outcomes in Breast Cancer Autotransplantation Patients.

Major findings from our research are presented in **manuscript number 3**. This paper represents the first time that we have adequate data to performed statistical analysis to determine if there are statistically significant differences between the CCSP treated group and the control group during hospitalization. While the findings reported in this study should be evaluated as preliminary, they are very convincing. A more detailed report of the findings are presented below.

Sample Characteristics

Fifty two (47 %) patients were in the a CCSP treated group and 58 were in the control group (Table 1). The majority of the patients were 41 to 50 years old. Ninety percent in the CCSP group compared to 57% in the control group were married ($P<0.001$). The CCSP group had a statistically significant lower annual household income ($p<0.05$) than the control group. Forty percent in the CCSP group compared to 21% in the control group had practiced some earlier coping methods ($p< 0.05$). There were no statistically significant differences between the groups with regard to stage of the disease and type of chemotherapy treatment (Fig. 1). The rate of patient accrual at follow-up since AT was not found to differ significantly between the two groups of subjects.

Pain

All mean pain intensity scores were low. The mean affective pain scores were slightly higher than the sensory scores on day +7 (table 2). The total mean pain score was lowest on day -2 for the treatment group, and reached a peak level on day +7. Pain scores gradually increased and reached their peak intensity level on day +7 for both the treatment and control groups. There were no significant differences between the groups with regard to the intensity of the different pain scores.

The most frequent words chosen by the subjects to describe the sensory component of pain were: aching (25%), sore (24%), Dull (13%). The most frequent affective words were annoying (26%); tiring (17%); troublesome (10%); and nagging (10%). Pain was most frequently located in the vagina (19%); chest (14%); shoulder (13%) and arm (10%).

Psychological Distress
Anxiety remained constant for the control group from baseline to day +7 but decreased by 9 points in the CCSP group from baseline to day +7. Depression increased in both groups over time and reached a peak level in the control group on day -2. There were no statistically significant differences between the groups with regard to psychological distress.

Nausea
In the CCSP group, nausea was more severe on day -2 than on day +7. The opposite was the case in the control group with nausea reaching it's greatest intensity level on day +7. On day +7 nausea was 23 points higher in the control group compared to the CCSP group. **There was a statistically significant difference between the groups regarding nausea on day +7 with the CCSP treatment group reporting less nausea than the control group F (1, 72) = 5.50, p<0.05). After controlling for demographic variables and the nausea score on day -2, there was still a group difference on day +7 with the CCSP group showing statistically significant lower scores than the control group (B=-16.94, Beta=-.28,p<0.05).** Nausea is a major problem for patients receiving chemotherapy and autotransplantation. The CCSP appears to be an effective treatment strategy against nausea.

Fatigue
Fatigue reached peak levels on day -2 for both groups with fatigue increasing by 10.80 points in the CCSP group from baseline to day -2 compared to 20.33 points in the control group. On day +7, the control group rated fatigue as 9.44 points higher than the CCSP group. There were no statistically significant differences in fatigue levels between the groups on day -2 . On day +7, after controlling for fatigue on day -2, there was a significant difference between the groups F (1, 63,) = 4.01, p<0.05. However, after controlling for demographic variables and fatigue on day -2, there were no statistically significant differences between the groups. **When an index of nausea + fatigue was created for day +7, and after controlling for demographic variables, there was a significant difference between the groups with the control group having higher scores B= -26.23, Beta-.27, p<0.05.** Fatigue is a major problem for breast cancer patients who receive chemotherapy and autotransplantation.

Gaston-Johansson, F., Nanda, J., Kennedy, J. (1998) The Effect of a Comprehensive Coping Strategy Program on mortality (to be submitted to Lancet or New England Journal of Medicine after review of manuscript by physicians working with breast cancer patients at the Johns Hopkins Oncology Hospital, a NCI designated National Center).
Manuscript number 4 examines the effect of the CCSP on mortality and survival. The sample characteristics are the same as in manuscript 3. A total of 16 patients (14.5%) had died when follow up was carried out. When stratified by group, 4 patients in the CCSP group (7.7%), compared to 12 in the control group[(20.7%) had died at follow up. **There were statistically significantly fewer deaths in the CCSP treated group than the control group (p<0.5). The mean survival period was 341 days for the CCSP group compared to 233 days for the control group at follow-up. The odds ratio for mortality among the CCSP group was 0.32 (p<0.05) (Table I). Breast cancer patients in the CCSP treated group were 8.5 (1.7-41.6), p<0.001, less likely to die than the breast cancer patients in the control group.**

Mortality
Table II (Appendix E) describes the distribution of metastatic stages, types of chemotherapy received, follow up period since receiving autotransplantation (AT) and potential sociodemographic risk factors and their association with mortality. It also displays the crude odds ratio and its 95% confidence interval for mortality between CCSP patients and controls. The CCSP patients were less likely to die than their controls. The patients who were followed up two to three years following the AT were 8.5 times more likely to die than those who had

their AT up to one year at follow up. A combined follow up period of one to three years placed the patients at a mortality risk of 4.5 (95% CI: 1.0-21.1; $p = 0.05$). Additionally patients who had a metastatic stage IV breast cancer were 9 times (95% CI: 1.0-77.5; $p < 0.05$) more likely to die than patients diagnosed with stage II disease. All of the above variables with significantly association with mortality, and traditional sociodemographic factors were subsequently entered into a multiple logistic regression model for measuring the final group differential in mortality. Table III shows that CCSP patients were 11% less likely to die (P=0.05) than the control patients when adjustments were made for demographics, metastatic stage, type of chemotherapy and previous practice of coping and relaxation methods, and follow up period of 2 to 3 years.

Figure 2 (Appendix E) presents the survival probabilities at follow-up since AT between CCSP and the control groups. In general, the CCSP group shows a better chance of survival than the control group. Furthermore, the control group had a larger decline in the survival slope between 200 to 400 days at follow up since AT than the CCSP group, thus widening the overall difference in survival between the groups at 3 year follow up.

Discussion

As hypothesized, patients with breast cancer who underwent bone marrow transplant and received the CCSP, where less likely to die than the comparison group (7.7% Vs 20.7%). This difference was both clinically and statistically significant. Trends in statistical significance between groups during the multivariate analytic phase were noted ($p = 0.05$). These results appear to indicate that the CCSP treatment may have been effective. It appears from our study, that the probability of survival did not diverge until about one year following AT. The demographic characteristics of the sample did not influence the findings related to mortality, non did the stage of the disease or the type of chemotherapy.

The results of survival between groups need to be interpreted with caution. All patients have not been in the study for the same length of time regardless of group assignment. The mean survival time which was 341 days for the CCSP group and 233 days for the control group (table I) could be a function of the patients' length of time in the study. For this reason we introduced follow up since AT as a covariate. Entry of this variable into the final model reduced the mortality likelihood for the CCSP group from 15% to 11% and lowering the p value from 0.06 to 0.05. It is possible to obtain statistically significant differences between groups in mortality once the participants have been in the study for a longer period of time than the current follow up period.

The emphasis of the CCSP was to help patients cope with multiple symptoms and stress while improving their quality of life and survival. At no time did our research team intend for the CCSP to influence the course of the disease or the mortality of the patients. A theoretical discussion is presented in the manuscript listed below along with tables and figures in an attempt to explain our results.

B. Results related to Objective 8

Gaston-Johansson, F., Lachica, E., (1998) The Effectiveness of A comprehensive Coping Strategy Program from The Patients' Perspective

Manuscript number 5 is presently being written and will be completed by the time the final report is due. This paper deals with the patient's evaluation of the CCSP. A summary of the findings that have been analyzed to date are presented below.

Benefits Effectiveness of the CCSP Intervention from the Patients Perspective

The CCSP intervention (handouts and audiotapes) was reinforced according to protocol in all subjects who remained in the study. In addition, patients were instructed to use the CCSP at least once a day during hospitalization on a routine basis. The patients in the treatment group were also instructed to identify other situations in which they felt that the CCSP intervention was helpful and to record in the diary the situation in which the CCSP handouts and audiotapes were used. The patients were also instructed to document whether or not the CCSP intervention was beneficial in relieving their symptoms.

It was interesting to note the time of day and the situations in which the patient chose to use the CCSP handouts and audiotapes. The most frequent use of the CCSP intervention was during the evenings around bedtime. The most frequent symptoms\problems for which the patients used the CCSP intervention were psychological problems(51%) and sleep problems (60%). Twenty one percent of the patients used the CCSP to deal with chemotherapy side effects. The CCSP handouts and audiotapes were used 385 times by the patients. Both the handouts and the audiotapes were beneficial based on the patients reports. However, the patients documented the CCSP audiotapes as more beneficial. The audiotapes were used over 50% more often than the handouts. Twenty one (78%) of the patients reported that the audiotapes were effective 90-100% of the time compared to 19 (70%) of the patients reporting that the handouts were beneficial 90 to 100% of the time. Four (15%) of the subjects found the handouts to be beneficial 50 - 89 % of the time compared to 6 (22%) of the subjects reporting the audiotape to be beneficial 50 - 89 % of the time. Four patients reported that the handouts were beneficial less than 50% of the time. The remaining subjects in the treatment group only indicated that they had used the CCSP according to protocol and did not record additional situations in which they had used the handouts and audiotapes.

The patients overwhelmingly reported that they found the CCSP intervention helpful. They used the CCSP intervention during critical points in their treatment and on days when they experienced most side effects from the ABMT and found the CCSP intervention to be helpful 90 to 100% of the time. The subjects used the CCSP in situations that are supported theoretically in the scientific literature for use of behavioral treatment strategies such as to decrease their psychological distress, to decrease side effects of chemotherapy, and to induce sleep. Although the CCSP was mainly used during the evenings, it was also frequently used during the afternoons.

The patients used the CCSP audio-tapes more frequently and found them to be more helpful than the CCSP handouts. The increased use of the audio-tapes may be explained by the fact that it is a procedure that has to be followed whereas the handouts support cognitive restructuring. Hopefully, the information in the handouts gradually becomes an automatic part of the subjects' thinking processes and therefore do not need to be read so frequently. The audio-tapes make relaxation possible through the participation of subjects in a carefully outlined progressive relaxation procedure combined with imagery. The audio-tapes are also designed to help the subjects become relaxed more quickly as they become more comfortable with the information and instructions on the tape.

The benefits derived from the CCSP, as experienced by the patients, have important implications for clinical practice. The effects of the CCSP may be helpful to a broader group of cancer patients who are treated with chemothearpy for breast cancer but do not receive the ABMT. The audiotape is inexpensive and can easily be used in a variety of situations to help cancer patients cope with psychological distress, and sleeplessness. Clearly, the breast cancer patients in the treatment group in this study have overwhelmingly acknowledged the benefits of the CCSP.

C. Statistical Analysis and Results Related to Objective 9

We tested the effectiveness of CCSP on the 12-month follow-up QOL measures by undertaking the following statistical/analytical steps:

1. Initial distribution and independent association of proportions to test differences between CCSP and control groups at baseline, by using chi-square tests. Mean differences between groups were also tested both at baseline and follow-up for all outcomes as well as co-variates .

2. Correlation between outcome scores at follow-up and baseline psychological scores were carried out by using zero-order correlations to determine strength of association. The extent of multi-colinearity among covariates, and interaction factors, if any existed, were also tested as a part of the second step.

3. Simple linear regressions assessed the influence of treatment at a crude level. Subsequent hierarchical regression models were tested by incrementally introducing different conceptually plausible factors while accounting for the subject's baseline status on the outcome(s), and by using analysis of covariance (ANCOVA) methods. Sequential steps in this phase of the analysis helped us determine the level of hierarchy where the CCSP had maximum effect on the overall QOL scores and its sub-scales. Such a step also gave us the advantage to assess the best fitting model that can be derived, within the limitations of the constructs available in the databases. Measures within each of the hierarchy were kept constant in order to compare and contrast the differences in the standardized coefficients and variance among total scores and sub-scales and also to assess the increment or decrement of the effectiveness of treatment.

Subjects

The sociodemographic characteristics at baseline of patients (CCSP, N=38, control, N=35) followed-up a year or more later are presented in Table 1. This subsample is comparable with the overall sample of 138 subjects. The major characteristics are that the subjects are 41 - 50 years of age, white, college graduate or higher, professional with incomes above $50,000. Most subjects had stage III breast cancer.

Confounding Variables

Psychological distress, Health Locus of Control and Coping Strategies were identified as confounding variables. Mean scores of these constructs are presented in Table 2. The anxiety scores indicated that the patients in both groups experienced mild anxiety at baseline. However, only the control group reported mild depression. The most frequently used coping strategy in both groups was coping self-statements.

Quality of Life

The mean and standard deviation scores on overall quality of life (QOL) scale and subscales between patients (controls and CCSP treated) at baseline and at one year or more follow-up are presented in Table 3. Psychological well-being was the only QOL subscale with a score below 20 in both groups. The CCSP treated group had a statistically significantly higher overall quality of life ($p<.05$), psychological well-being, socioeconomic well-being ($p<.05$), and spiritual well-being ($p<.01$) than the control group at follow-up (Table 3).

As expected, there were significant correlations among the overall QOL and subscales of QOL. With the exception of a significant correlations between state anxiety and socioeconomic and family well-being, all other QOL scales were statistically significantly correlated to state and trait anxiety and depression (Table 4). There were no significant correlations between health locus of control variables and overall QOL and the subscales of QOL. Coping self-statements, reinterpretation and avoidance of catastrophe were significantly related to different QOL scales (Table 4).

Effectiveness of the CCSP

A model measuring the effectiveness of the CCSP on Quality of Life (total and subscale scores) constructs at follow-up a year or more after autotransplant among patients with breast cancer is presented in Table 5. The CCSP treated group showed significant improvement in overall QOL (Beta=0.31, $p<.01$), psychological well-being (Beta=0.24, $p<.05$), social well-beling (Betas=0.25, $p<.05$), and spiritual well-beling (Beta=0.36, $p<.01$) than the control group without any adjustment factor. With incremental adjustment for baseline QOL, disease stage, chemotherapy type, demographics, trait anxiety, coping self-statements and avoidance of catastrophe, and internal/powerful others locus of control and depression (Table 5). The results showed that the CCSP improved the QOL (Beta=0.26, $p<.05$; R^2= 49%), psychological well-being (Beta=0.28, $p<.05$; R^2 =51%) and spiritual well-being (Beta=0.39, $p<.05$; R^2=39%) of breast cancer patients at one year follow-up and more after an autotransplant.

D. A summary of findings related to Objective 1: Primary Caregivers

Demographics

One hundred and two PCGs participated in the study (55 in the CCSP treated group and 47 in the control group). The majority of the PCGs for breast cancer patients were male, white, married, college graduates, and protestants (Table 6). They had incomes above $50,000, were professionals and worked full time.

A comparison of means and standard deviations between treatment and control groups for selected variables can be found in Table 7. Both groups experienced moderate anxiety (Table 8). Neither of the groups experienced depression. All other scores were similar and there were no statistically significant differences between the control and CCSP treatment groups ratings of fatigue, depression, anxiety, quality of life, burden of care and locus of control at baseline.

Anxiety and fatigue were more severe in females and PCGs who were single ($p<0.05$ to $p<0.01$). Family, a subscale of quality of life was predictive of burden of care (Beta= -2.45, $p<0.05$). Follow-up data for PCGs will be analyzed during the final year of the study (Tables 9 and 10).

E. A summary of findings related to Objective 2: Primary Caregivers

Data related to Objective 2 will continue to be collected and analyzed during the final year of the project.

VII. Summary of Findings for Patients

Our research team has met the goals set forth and approved in our annual report of August, 1997.
We have been able to show that women who undergo autotransplantation suffer from multiple symptoms that have a significant impact on their health status. The women who received the CCSP experienced significantly less intense nausea and fatigue + nausea on day +7 when they are sickest and less able to manage adverse symptoms, than the control group. The patients who were treated with the CCSP lived significantly longer

and had a statistically significantly higher quality of life than the patients who did not receive the CCSP. Our data supports the CCSP as an effective treatment strategy.

VIII. Extension of Project

This project has been extended until August 31, 1999. The following tasks will be completed during the extension period.

1. Collection of follow-up data in both patients and PCGs: September to February 1999.
2. Data analysis: March to April 1999.
3. Writing of manuscripts for publication: May to August 1999.
4. Preparation of final report: July to August 1999.

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APPENDIX A

A Comprehensive Coping Strategy Program

Presentation: A variety of teaching strategies are used to present the Comprehensive Coping Strategy Program (CCSP) to help promote and maintain breast cancer ABMT patient and PCG interest. Patients, particularly in clinical settings, are likely to experience a range of physical and psychological factors, such as pain, fatigue and anxiety resulting from high psychological stress, which compete with the educator for their interest levels 43. Consideration was also given to providing the best match between specific content areas and the most appropriate teaching. Oral communication (lecture) has been found most effective in establishing rapport and in teaching new knowledge such as preparatory information, while slide tapes are especially beneficial for abstract concepts. Videotapes are most effective in situations when learning step-by-step procedures with movement is required, such as relaxation techniques with guided imagery 43-44. A conference/treatment room is used to present the CCSP. This setting has comfortable chairs and adequate space to practice relaxation. The setting is also appropriate for presenting educational materials.

Preparatory Information: The purposes of the CCSP are presented by the instructor using an overhead. A schematic drawing of the symptoms (pain, psychological distress, and fatigue) that patients are known to experience is presented. The instructor reviews the overhead pointing out the relationship among the different symptoms and how they can influence each other. The instructor summarizes the information by stressing that adequate control of pain can lead to decreased psychological distress and a decrease in physical symptoms other than fatigue. The subjects are told that the information presented is based on the experiences of patients who have successfully undergone ABMT. Handouts that cover appropriate information are reviewed and given to the participants: 1) "Ways in Which You Can Participate in Reducing Pain and Psychological Distress, and; 2) "Some General Ways To Increase Control". The above information is presented by the instructor using simple terminology and principles of learning. In order to make sure that the content is presented in a standardized manner, a detailed script and specific overheads are used by the instructor to present this material.

Treatment of Pain: Theoretical Considerations: This part of the CCSP is a slide presentation with an accompanying tape. Interaction between the instructor and the participants is also encouraged. Information covered include the following topics: definition of pain; the three components of pain; a brief explanation of the Gate Control Theory and; theoretical reasons why increasing control through use of coping self-statements and relaxation with imagery can relieve pain and emotional distress. A handout, titled "Ways in Which You Can Participate In Reducing Pain" is reviewed by the instructor and given to the participants at the end of the session. Colorful slides of simple pictures, that symbolize neuro-physiological structures are used when the Gate Control Theory is presented.

Cognitive Restructuring: This segment of the CCSP is also a slide presentation with accompanying tape. This information focuses on the avoidance of catastrophizing, distorted thinking and the use of positive coping self-statements. Cognitive restructuring is directed at modifying thought processes in order to lessen negative sensations and psychological distress. The subjects are taught to conduct an internal dialogue with themselves which directs and refocuses their attention and thinking. This includes descriptions of unproductive catastrophizing statements made by people experiencing discomfort and distress, and then alternatives that may prove more useful in coping. This includes statements such as "I feel relaxed", "I am in control and can handle this situation" and "I know any discomfort I may feel won't last forever". Two handouts, titled "15 Styles of Distorted Thinking to Avoid", and "15 Positive Coping Self-Statements," will be reviewed by the instructor and given to the participants.

Relaxation With Imagery: This part of the CCSP is presented on video-tape in a participant modeling format in which each component of relaxation will be briefly presented, described and demonstrated. The treatment includes a brief progressive muscle relaxation procedure with tense-release cycles being used with specific muscle groups (face, neck and shoulders, stomach and chest, arms and legs). Following these cycles, cue-controlled relaxation will be used involving deep breathing and saying the word "relax" to begin to develop an association between a state of relaxation and these cues. With practice, the cues can then be used to achieve a state of relaxation in a much shorter period of time. Imagery is introduced into the relaxation exercise and participants are permitted to choose the imaginary scene. At the end of the session, the instructor reviews two handouts and gives them to the participants. The handouts are: "Learning and Using Relaxation Therapy" and "Benefits of Relaxation Therapy". The instructor will also give the patient and PCG a small hand-held audiotape recorder (Walkman) with two sets of ear phones and an audiotape. The purpose of the tape is to guide the participants in active participation in the relaxation exercise. The participants are instructed to review all handouts and to practice the relaxation exercise, using the 15 minute audiotape at least every day and prior to stressful events. The subjects are instructed how to review the handouts and record their use of the audiotape in a diary.

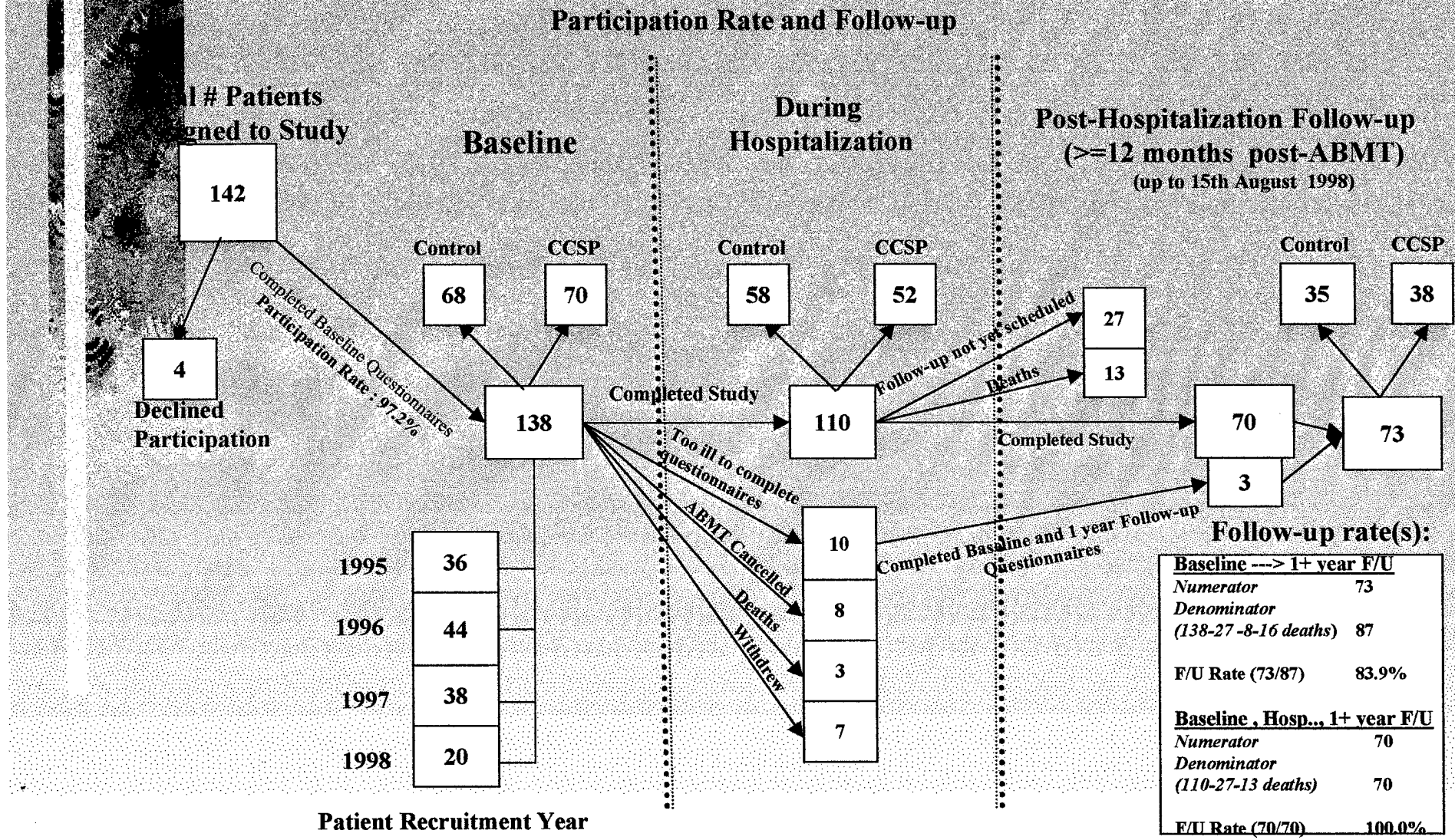
Reinforcement of CCSP: The reinforcement of the CCSP includes: review of the patients and PCGs diaries, responding to any questions that the subjects have concerning the CCSP; measuring relaxation prior to and post reinforcement of the CCSP; reviewing all handouts with the subjects; and having the subjects listen to the 15 minute audiotape with the relaxation exercise with imagery. Reinforcement of the CCSP takes about 30 minutes.

Figure 1

Effectiveness of a Comprehensive Coping Strategy Program(CCSP) on Health Status and Quality of Life of Patients with Metastatic Breast Cancer Receiving Autotransplant (ABMT):1995-1998

Ongoing Collaborative Intervention Study by the Johns Hopkins Medical Institutions: Johns Hopkins Hospital and Johns Hopkins School of Nursing

(Sponsor: U.S. Armed Force Medical Services)



Updated: 1st September, 1998 (JN090198: d:\ssiz1c)

Table 1
Socio-demographic characteristics at Baseline of Patients (CCSP and Controls) followed up a year or more later

Characteristics		Controls		CCSP		Total	
		N	%	N	%	N	%
Age	22-40 years	11	32.4	9	23.7	20	27.8
	41-50 years	19	55.9	18	47.4	37	51.4
	51 years and above	4	11.7	11	28.9	15	20.8
Ethnicity	White	30	85.7	34	89.5	64	87.7
	Non-white	5	14.3	4	10.5	9	12.3
Education	High school or less	7	20.6	3	7.9	10	13.9
	Some College	12	35.3	8	21.1	20	27.8
	College grad or higher	15	44.1	27	71.1	42	58.3
Annual Income	Less than 50K	15	42.9	9	23.7	24	32.9
	50K or greater	20	57.1	29	76.3	49	67.1
Marital Status*	Single	14	40.0	4	10.5	18	24.7
	Married	21	60.0	34	89.5	55	75.3
Employment	Not employed	13	37.1	8	21.1	21	28.8
	Employed	22	62.9	30	78.9	52	71.2
Occupation	Non-Professional	16	45.7	12	31.6	28	38.4
	Professional	19	54.3	26	68.4	45	61.6
Metastatic Stage	Stage II	9	25.7	5	14.7	14	20.3
	Stage III	15	42.9	19	55.9	34	49.3
	Stage IV	11	31.4	10	29.4	21	30.4
Chemotherapy Type	Type I	23	65.7	17	50.0	40	58.0
	Type II	12	34.3	17	50.0	29	42.0

* $P<0.05$

Table 2
Mean (± s.d.) Scores at Baseline on Anxiety, Depression, Health Locus of Control and Coping Strategies Scales and Subscales Among Patients (CCSP and Controls) followed up a year or more later

Constructs		Controls		CCSP		Total	
		Mean	s.d.	Mean	s.d.	Mean	s.d.
Anxiety	State	39.7	10.5	39.9	11.2	39.8	10.8
	Trait	38.1	9.2	36.9	8.7	37.5	8.9
Depression		11.9	8.4	9.9	6.0	10.8	7.3
Health Locus of Control	Internal	24.8	5.0	23.9	4.1	24.3	4.6
	Powerful others	16.3	4.9	16.8	5.5	16.6	5.2
	Chance	21.4	4.7	20.6	6.1	21.0	5.4
Coping Strategies	Ignoring Pain	14.6	7.7	15.5	8.1	15.1	7.9
	Coping Self-statements	23.0	6.0	21.9	6.1	22.4	6.0
	Reinterpretation	7.0	6.9	7.1	6.8	7.1	6.8
	Diverting Attention	15,3	8.4	18.1	7.9	16.8	8.2
	Praying	18.3	7.5	18.8	8.7	18.5	8.1
	Behavioral Adaptation	16.9	6.0	18.2	5.3	17.6	5.6
	Avoidance of Catastrophy	30.2	5.5	30.5	5.3	30.4	5.3
	Overall Coping	125.3	26.6	130.1	31.0	127.8	28.9

Table 3
Mean (± s.d.) Scores on Quality of Life (QOL) Scales and Subscales Among Patients (CCSP and Controls) followed up a year or more later

QOL Constructs		Controls		CCSP		Total	
		Mean	s.d.	Mean	s.d.	Mean	s.d.
Overall QOL	Baseline	20.6	4.1	22.6	4.3	21.6	4.3
	Follow-up**	21.9	5.0	24.7	3.6	23.4	4.5
Psychological Well-being	Baseline	18.2	5.5	19.6	6.1	18.9	4.3
	Follow-up*	20.2	5.9	23.0	5.7	21.6	5.9
Socioeconomic Well-being	Baseline*	22.7	4.8	24.9	3.5	23.9	4.3
	Follow-up*	23.4	4.9	25.5	3.6	24.5	4.4
Spiritual Well-being	Baseline	21.3	5.3	23.6	4.6	22.5	5.0
	Follow-up**	21.3	7.2	25.7	3.9	23.6	6.1
Family Well-being	Baseline*	23.7	5.1	26.3	4.8	25.1	5.1
	Follow-up	26.2	4.1	27.7	3.2	27.0	8.9

* $P<0.05$ ** $P<0.01$

Table 4
Correlation of Baseline Scores on Quality of Life (QOL), Anxiety, Depression, Health Locus of Control and Coping Strategies Constructs with QOL Constructs at Follow-up Among Patients (CCSP and Controls)

Baseline Constructs		QOL Follow-up				
		Total	**PWB**	**SoWB**	**SpWB**	**FWB**
Overall QOL (Total)		0.62**				
Psychological Well-being (PWB)		0.56**	0.57**			
Socioeconomic Well-being (SoWB)		0.45**	0.29*	0.63**		
Spiritual Well-being (SpWB)		0.51**	0.45**	0.42**	0.54**	
Family Well-being (FWB)		0.38**	0.35**	0.27	0.28*	0.45**
Anxiety	State	-0.23	-0.24*	-0.12	-0.27*	0.01
	Trait	-0.47**	-0.41**	-0.29*	-0.51**	-0.23
Depression		-0.42**	-0.40**	-0.28*	-0.39**	-0.22
Health Locus of Control	Internal	-0.06	-0.05	-0.07	-0.04	-0.01
	Powerful others	-0.13	-0.09	-0.02	-0.23	-0.07
	Chance	-0.07	-0.08	-0.06	-0.03	0.04
Coping Strategies	Ignoring Pain	0.18	0.21	0.19	0.04	-0.01
	Coping Self-statements	0.13	0.12	0.25*	-0.03	0.05
	Reinterpretation	-0.06	-0.08	0.07*	-0.11	-0.04
	Diverting Attention	0.04	0.01	0.10	0.09	-0.10
	Praying	-0.12	-0.12	-0.21	0.03	-0.80
	Behavioral Adaptation	0.08	0.06	0.10	0.10	-0.05
	Avoidance of Catastrophy	0.40**	0.35**	0.41	0.33**	0.16
	Overall Coping	0.13	0.11	0.18	0.09	-0.03

* P<0.05 ** P<0.01

Table 5
Hierarchical ANCOVA models measuring the effectiveness of CCSP on Quality of Life (Total and Subscores) constructs at follow-up a year or more after autotransplant Among Patients with Metastatic Breast Cancer (N=73)

Models Tested with Incremental Adjustment Factor(s)	QOL Follow-up									
	Overall QOL		Psychological Well Being		Social Well Being		Spiritual Well Being		Family Well Being	
	Beta@	Adj.R^2	Beta@	Adj.R^2	Beta@	Adj.R^2	Beta@	Adj.R^2	Beta@	Adj. R^2
1. Unadjusted	0.31**	0.08	0.24*	0.04	0.25*	0.05	0.36**	0.12	0.20	0.03
2. Baseline QOL	0.15	0.38	0.15	0.33	0.08	0.39	0.22*	0.32	0.09	0.18
3. (2) + Disease stage, chemotherapy type	0.18	0.39	0.19	0.35	0.05	0.35	0.26*	0.29	0.15	0.16
4. (3) + Demographics	0.59**	0.48	0.57**	0.47	0.60**	0.41	0.30*	0.32	0.48**	0.16
5. (4) + Trait Anxiety	0.22	0.47	0.23*	0.46	0.02	0.40	0.33*	0.37	0.18	0.16
6. (5) + Coping Self-Statements and Avoidance of Catastrophy	0.26*	0.49	0.26*	0.47	0.05	0.43	0.37**	0.40	0.20	0.16
7. (6) + Internal/Powerful Others LOC	0.26*	0.49	0.26*	0.50	0.04	0.41	0.37**	0.37	0.20	0.13
8. (7) + Depression	0.26*	0.49	0.28*	0.51	0.03	0.41	0.39**	0.39	0.19	0.11

@ standardized coefficient * P<0.05 ** P<0.01

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Table 6 Demographic characteristics of primary care givers (Frequency)

Group Assignment	Count	Cumulative Count	Percent	Cumulative Percent
1: Treatment Group	55	55	53.92	53.92
2: Control Group	47	102	46.08	100.00
SEX				
1: Female	25	25	24.51	24.51
2: Male	77	102	75.49	100.00
RACE				
1: White	89	89	87.25	87.25
2: African American	9	98	8.82	96.08
3: Hispanic	1	99	.98	97.06
5: Asian	2	101	1.96	99.02
6: Other	1	102	.98	100.00
MARITAL Status				
1: Married	92	92	90.20	90.20
2: Single	9	101	8.82	99.02
3: Widowed	1	102	.98	100.00
Education				
1: Grade School	2	2	1.96	1.96
2: High School	19	21	18.63	20.59
3: Some College	26	47	25.49	46.08
4: College Graduate	36	83	35.29	81.37
5: Graduate Degree	19	102	18.63	100.00
RELIGION				
1: Catholic	23	23	22.55	22.55
2: Protestant	47	70	46.08	68.63
3: Jewish	5	75	4.90	73.53
4: Other	16	91	15.69	89.22
5: None	9	100	8.82	98.04
Patient lives with:				
1: Spouse	89	89	87.25	87.25
2: Significant other	3	92	2.94	90.20
5: Self	9	101	8.82	99.02
Missing	1	102	.98	100.00
INCOME				
1: less than $20K	4	4	3.92	3.92
2: $20-29K	8	12	7.84	11.76
3: $30-39K	5	17	4.90	16.67
4: $40-49K	15	32	14.71	31.37
5: more than $50K	65	97	63.73	95.10
Missing	5	102	4.90	100.00

Table 6 Demographic characteristics of primary care givers (Frequency - continued)

Occupation	Count	Cumulative Count	Percent	Cumulative Percent
1: Professional	62	62	60.78	60.78
2: Technical	13	75	12.75	73.53
3: Retired	12	87	11.76	85.29
4: Other	15	102	14.71	100.00
Employment Status				
1: Full-time	78	78	76.47	76.47
2: Part-time	7	85	6.86	83.33
3: Unemployed-resigned	5	90	4.90	88.24
4: Unemployed -Disability	2	92	1.96	90.20
5: Unemployed -Retired	8	100	7.84	98.04
Missing	2	102	1.96	100.00

Table 6 Demographic characteristics of primary caregiver (Descriptive statistics)

	Valid N	Mean	Minimum	Maximum	STD
AGE	102	47.59	25	73	10.76

Table 7 Sample characteristics of primary caregiver (Descriptive statistics)

	Valid N	Mean	Minimum	Maximum	STD
Fatigue Intensity	102	16.20	0.00	71.92	16.83
Temporal	102	31.43	0.00	90.50	21.13
Affective	97	32.00	0.00	90.60	24.73
Sensory	101	36.04	0.00	76.58	20.72
Total	102	28.52	0.00	75.38	18.46
Depression	102	7.83	0.00	26.00	5.69
State Anxiety	101	40.28	22.00	64.00	10.92
Trait Anxiety	101	37.40	24.00	58.00	7.91
QOL Health	101	8.43	1.50	23.86	4.27
Socioeconomic	101	7.25	0.00	18.67	4.18
Spiritual/psychological	100	7.81	0.00	20.86	4.55
Family	100	8.77	0.00	24.00	5.45
Objective Burden	102	32.49	23.00	42.00	3.93
Subjective Burden	101	31.27	19.50	47.00	5.44
Health Locus Control ILHC	101	26.04	17.00	36.00	3.97
PHLC	101	17.17	6.00	30.00	5.49
CHLC	101	20.67	8.00	31.00	4.42

Table 8 Comparison of means of selected variables between treatment and control groups

	1. Treatment Group			2. Control Group			t-	df	p
	Mean	N	STD	Mean	N	STD	value		
Fatigue Inten	16.96	55	17.28	15.31	47	16.42	.492	100	.624
Temporal	33.56	55	22.50	28.94	47	19.34	1.103	100	.273
Affective	32.91	51	26.94	30.99	46	22.30	.380	95	.705
Sensory	37.63	54	21.04	34.21	47	20.41	.827	99	.410
Total	29.63	55	19.37	27.21	47	17.46	.659	100	.511
Depression	8.14	55	6.10	7.46	47	5.21	.596	100	.553
State anxiety	40.19	55	9.87	40.39	46	12.17	-.093	99	.926
Trait Anxiety	37.29	54	8.19	37.52	47	7.68	-.146	99	.884
QOL Health	8.84	54	4.37	7.95	47	4.13	1.04	99	.299
Socioeco	7.20	54	3.94	7.30	47	4.48	-.12	99	.906
Spiritual/psy	8.05	54	4.49	7.53	46	4.65	.57	98	.568
Family	8.96	54	5.56	8.56	46	5.38	.36	98	.720
Obj Burden	32.67	55	3.90	32.27	47	3.99	.51	100	.614
Subj Burden	31.23	54	5.49	31.31	47	5.45	-.07	99	.947
Control ILHC	25.56	54	3.98	26.60	47	3.93	-1.313	99	.192
PHLC	17.57	54	5.19	16.71	47	5.84	.783	99	.435
CHLC	20.17	54	4.69	21.25	47	4.07	-1.227	99	.223

Table 9 Comparison of selected variables by marital status +

	Married			Other			t-value	df	p
	Mean	Valid N	STD	Mean	Valid N	STD			
AGE	48.21	92	10.19	41.90	10	14.43	1.780	100	.078
SEX	**1.80**	**92**	**.40**	**1.30**	**10**	**.48**	**3.720**	**100**	**.000**
RACE	1.11	92	.31	1.30	10	.48	-1.731	100	.086
EDUC	3.55	92	1.03	3.00	10	1.25	1.582	100	.117
INCOME	**4.49**	**88**	**.97**	**2.78**	**9**	**1.64**	**4.683**	**95**	**.000**
WORK	1.34	90	.71	1.60	10	.97	-1.045	98	.298
PIPINTS2	15.85	92	16.75	19.41	10	18.15	-.634	100	.528
PIPTEMP2	30.40	92	20.93	40.86	10	21.68	-1.495	100	.138
PIPAFFC2	30.82	87	25.52	42.24	10	13.11	-1.389	95	.168
PIPSENS2	**34.47**	**91**	**20.75**	**50.34**	**10**	**14.49**	**-2.351**	**99**	**.021**
PIPTOT2	27.46	92	18.60	38.21	10	14.57	-1.766	100	.080
BECKTOT2	7.23	92	5.50	10.22	10	4.86	-1.644	100	.103
STAITTO2	**39.35**	**91**	**10.65**	**48.77**	**10**	**10.04**	**-2.668**	**99**	**.009**
TOTRAIT2	**36.94**	**91**	**7.84**	**41.60**	**10**	**7.71**	**-1.787**	**99**	**.077**
HEALTH2	8.74	91	6.22	8.77	10	7.16	-.012	99	.991
SOCIOEC2	8.86	91	6.20	8.76	10	6.92	.047	99	.962
SPIRIT2	8.77	91	6.27	8.71	10	7.28	.026	99	.980
FAMILY2	8.18	91	6.90	7.01	9	7.21	.481	98	.631
OBJBURD2	32.69	92	3.96	30.63	10	3.23	1.591	100	.115
SUBBURD2	30.95	91	5.24	34.13	10	6.66	-1.768	99	.080
ILHC2	26.08	91	4.13	25.70	10	2.11	.285	99	.776
PHLC2	17.35	91	5.55	15.60	10	4.88	.955	99	.342
CHLC2	20.87	91	4.50	18.86	10	3.31	1.368	99	.174

+ **Bold-faced** differences are statistically significant at $p < .05$.

* The recoding scheme is the same as before.

Table 10 Comparison of selected variables between female and male caregivers +

	Female			Male			t-value	df	p
	Mean	Valid N	STD	Mean	Valid N	STD			
AGE	49.56	25	14.04	46.95	77	9.48	1.056	100	.294
RACE*	1.20	25	.41	1.10	77	.31	1.249	100	.214
MARITAL*	**1.28**	**25**	**.46**	**1.04**	**77**	**.19**	**3.720**	**100**	**.000**
EDUC	**2.80**	**25**	**1.00**	**3.73**	**77**	**.98**	**-4.084**	**100**	**.000**
INCOME*	**3.67**	**24**	**1.55**	**4.55**	**73**	**.90**	**-3.428**	**95**	**.001**
WORK*	**1.96**	**24**	**.95**	**1.18**	**76**	**.53**	**5.028**	**98**	**.000**
PIPINTS2	19.94	25	17.66	14.98	77	16.49	1.28	100	.202
PIPTEMP2	36.14	25	19.17	29.90	77	21.62	1.29	100	.201
PIPAFFC2	32.40	25	19.57	31.86	72	26.41	.09	95	.925
PIPSENS2	39.03	25	20.78	35.06	76	20.74	.83	99	.408
PIPTOT2	31.88	25	16.61	27.43	77	19.00	1.05	100	.298
BECKTOT2	9.32	25	5.43	6.94	77	5.42	1.90	100	.060
STAITTO2	**44.28**	**25**	**11.31**	**38.96**	**76**	**10.53**	**2.15**	**99**	**.034**
TOTRAIT2	**41.25**	**25**	**6.92**	**36.13**	**76**	**7.85**	**2.91**	**99**	**.005**
HEALTH2	9.51	25	7.08	8.49	76	6.03	.70	99	.486
SOCIOEC2	9.55	25	6.87	8.62	76	6.05	.64	99	.521
SPIRIT2	9.38	25	7.17	8.56	76	6.08	.55	99	.580
FAMILY2	8.77	24	7.62	7.86	76	6.69	.56	98	.576
OBJBURD2	32.33	25	4.42	32.54	77	3.78	-.23	100	.819
SUBBURD2	30.68	25	5.65	31.46	76	5.39	-.62	99	.534
ILHC2	25.96	25	4.21	26.07	76	3.92	-.12	99	.906
PHLC2	17.32	25	6.25	17.13	76	5.26	.15	99	.879
CHLC2	21.62	25	4.16	20.36	76	4.49	1.25	99	.215

+ **Bold-faced** differences are statistically significant at $p < .05$.
* The recoding scheme is the same as before.

PIPSENS2	PFS Sensory Dimension scale
PIPTOT2	Total Scale
BECKTOT2	Beck Depression Scale
STAITTO2	State Anxiety Scale
TOTRAIT2	State Trait Scale
HEALTH2	QOL: Health and Functional subscale
SOCIOEC2	QOL: Socioeconomic subscale
SPIRIT2	QOL: Psychological Spiritual subscale
FAMILY2	QOL: Family subscale
OBJBURD2	Burden of Care: Objective
SUBBURD2	Burden of Care: Subjective
ILHC2	Multidimensional Health Locus of Control: Internal
PHLC2	Multidimensional Health Locus of Control: Powerful others
CHLC2	Multidimensional Health Locus of Control: Chance

Appendix B

Fatigue, Pain, and Depression as Predictors of Health Status in Breast Cancer Patients

Role of Symptoms in Health Status

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Abstract

PURPOSE: The purpose of this study was to determine the influence of fatigue, pain, and depression on health status in breast cancer patients who had completed adjuvant chemotherapy.

DESCRIPTION OF STUDY: A predictive, correlational design was used. A convenience sample of 127 women with stage II, stage III, or stage IV breast cancer was recruited. The setting was an urban National Cancer Institute designated comprehensive cancer center located in the Eastern United States. Standardized questionnaires and the Painometer© were used to measure the variables. The subjects completed questionnaires in the outpatient clinic. Relationships between the multiple dimensions of fatigue and pain, depression and health status were examined. Hierarchial regression techniques were used to determine the variance in health status accounted for by fatigue, pain, and depression.

RESULTS: The subjects ages ranged from 22 years to 60 years ($\underline{M} = 45 \pm 7.6$), were primarily married Caucasians with an average yearly household income of equal to or over $50,000. The sample was primarily Protestant, college educated, and employed in a professional position. All subjects had received previous surgery and adjuvant chemotherapy. Ninety-one percent reported fatigue as measured by the Fatigue VAS. Forty-seven per cent of the participants reported pain as measured by the POM-VAS. Although the mean scores were low for sensory, affective, total , and overall pain intensity, the range of reported pain scores was wide indicating that some subjects did experience moderate to severe pain intensity. Fifty-four percent of the participants reported depression, ranging from mild (30%), to moderate (19%), to severe/high (5%). Subjects reported a mean total perceived health status rating of 50.73 (SD = 10.79). The variables of interest (fatigue, pain, and depression) were all significantly correlated to each other and to total health status.

Variance in health status was determined after controlling for demographic variables. Depression ($p < .001$) and pain ($p < .01$) significantly accounted for 64% (adjusted $R^2 = .60$) of the variance in total health status. Fatigue ($p < .05$) and depression ($p < .001$) accounted for 42% (adjusted $R^2 = .36$) of the variance in the perception of health status.

CLINICAL IMPLICATIONS: Multiple symptoms are experienced by breast cancer patients who are treated with chemotherapy following mastectomy. Women with breast cancer who receive adjuvant chemotherapy will most likely experience fatigue, pain, depression, and alterations in health status after treatment completion. Pain and depression had a significant impact on a woman's total health status where as depression and fatigue had an influence on perceived health status. Of the different dimensions of health status, one's perceptions of health status had the strongest correlation to total health status ($r = .84$, $p < .001$). Health care professionals need to be aware of the effects of multiple symptoms on health status and provide appropriate care to alleviate them.

KEY TERMS: fatigue; pain; depression, health status; breast cancer; adjuvant chemotherapy

Breast cancer in the United States is estimated to be diagnosed in 187,700 women in 1998; 43,500 women are predicted to die from this disease. [1] Survival rates in breast cancer correlate with the extent of disease, as evidenced by the ten year survival rate of 65% to 80% for women with disease confined to the breast decreasing to a median survival rate of approximately 2 years and a 2% to 5% probability of 5-year disease-free survival for women with metastatic disease.[2] Mastectomy followed by adjuvant chemotherapy for breast cancer is one treatment modality developed in response to the challenge of extending disease-free survival and survival. However, multiple symptoms such as fatigue, pain, and depression result from the treatment and may have a significant effect on the patient's health status. The purpose of this study was to determine if fatigue, depression, and pain were significant predictors of health status in breast cancer patients who had completed adjuvant chemotherapy. The study had the following research objectives:

1. To describe the prevalence and severity of fatigue, pain, depression, and alterations in health status in breast cancer patients with metastatic disease; and
2. To determine if fatigue, pain, and depression are significant predictors of health status.

Literature Review

Fatigue

Fatigue is the most commonly reported symptom associated with cancer. [3] Fatigue is a major debilitating symptom which can have a dramatic effect on the lives of breast cancer patients. [4] The nature of fatigue is complex, has been described by patients as weakness, weariness, sleepiness, tiredness, lack of energy, exhaustion, lethargy, and malaise [5] and may be a symptom of many diseases. [6] Aisters (1987)[7] conceptualized fatigue as a response to continual stress related to multiple physiological, psychological, and situational factors which are part of the disease and its treatment.

This conceptualization was supported by findings of Blesch, Paice, Wickham et al. (1991)[8] from a study examining correlates of fatigue in people with breast or lung cancer. Fatigue was described from a multidimensional perspective: pathophysiologically as an indicator of functional or metabolic disorder; physically in regard to a decrease in physical performance; and psychologically, as it relates to anxiety, depression, or boredom. [8]

Fatigue is a serious iatrogenic side effect associated with chemotherapy with cell destruction end products, nausea, and vomiting thought to be contributing factors. [9] Chemotherapy-related fatigue is cyclical, usually beginning 1 to 2 weeks post-chemotherapy administration in conjunction with the hematological nadir, decreasing, and then beginning with the following subsequent cycle. [10] Piper, Lindsey, and Dodd (1987)[11] noted that chemotherapy which crosses the blood-brain barrier and/or has neurotoxic properties may affect neurotransmission and thus produce fatigue. Sitzia and Huggins[12] reported a mean incidence of 89% in a sample of breast cancer patients treated with CMF. Potempka[13] in a review of nursing literature from 1978 through 1993 focusing on chronic fatigue in cancer patients receiving chemotherapy, found 18 reports of fatigue prevalence, intensity, and correlates. Prevalence estimates derived from several of these fatigue studies ranged from 80% to 99% (Potempka, 1993).[13] Fatigue may lead to patient abandonment of treatment, limited doses of chemotherapy, and decreased patient quality of life (QOL).[5]

Fatigue and its affects on mood, concentration, and activities of daily living has primarily been investigated relating to chemotherapy and radiation therapy. Few studies have examined the fatigue experience longitudinally from one treatment modality up through and in preparation for another treatment modality. There is also a paucity of research regarding the subjective nature of fatigue. Few studies have investigated fatigue's effect on overall health status, and instead have concentrated on

correlates such as psychological distress.

Research conducted by Blesch et al. [8] revealed that scores on the Profile of Moods States subscales for fatigue-inertia, tension-anxiety, depression-dejection, anger-hostility, and confusion-bewilderment were significantly correlated with self-rated fatigue intensity, and were inversely correlated with the vigor-activity subscale score in a sample of patients receiving chemotherapy and/or radiation therapy for breast or lung cancer. Similarly, Irvine, Vincent, Graydon, Bubela, and Thompson [14] found that fatigue covaried with symptom distress, mood disturbance, and loss of ability to perform usual functional abilities, and was not significantly correlated either with duration of disease status or with stage of disease.

The understanding and management of fatigue is clearly one of the greatest challenges to oncology nurse researchers and clinicians today.[15]

Pain

Pain has been shown to be a significant problem for breast cancer patients.[16-18] Pain may be acute, as experienced prediagnosis, following lumpectomy or mastectomy and axillary node dissection, or may be chronic and long-term in nature.[19] Treatment-related breast pain from surgery and chemotherapy is related to breakdown of the skin integrity. This treatment-related pain has been characterized as irritating ,[19] constricting, burning, or throbbing sensations localized to the posterior arm, axilla, and anterior chest wall. [20, 21]

Only one published study to date could be found that examined the pain experienced by breast cancer patients and its effects on their lives in the outpatient setting.[17] The study results found that 47% of breast cancer patients receiving treatment in the outpatient setting reported cancer-related pain. The majority of patients in this group were found to have treatment-related pain from post-

surgical neuropathic pain syndrome (56%) and cancer-related pain from bone metastasis (26%). Patients rated their pain as moderate to severe on a daily basis. Baron[20] reviewed the literature regarding sensory alterations experienced after breast cancer surgery. Results showed that many patients experienced a variety of sensory alterations in the breast area and the anatomical areas located near the breast - the chest wall, the arm, and the axilla. [20] These sensations, which included pain, were often reported as severe and distressing.[20]

Patients who experience cancer pain are found to have significantly more depression and anxiety, and more decreased QOL scores than pain-free patients.[22] Cancer survivors have noted that fatigue was a precursor to decreasing their tolerance to pain and that pain is a physical symptom related to increasing fatigue.[23]

Depression

Depression is a common response to the diagnosis of and treatment for breast cancer. [24, 25] Massie (1990)[26] found from an analysis of 20 years of research regarding depression in cancer patients that approximately 25% were depressed and up to 50% exhibited some symptoms of depression.

Coscarelli-Shag et al.[27] identified the following major sources of psychological distress for breast cancer patients at one month post-diagnosis: a) anxiousness while waiting for test results and having to undergo additional diagnostic tests; b) worries over whether the cancer was progressing; c) concern about ability to take care of self; and d) concern about how the family would manage if the patient died. Adjuvant chemotherapy represents a prolonged threat to a patient's mortality and functioning leading to additional psychological distress after breast surgery. Elevated levels of depression and anxiety may persist in a minority of breast cancer patients even years after the diagnosis.[28]

Spiegel, Sands, and Koopman[29] explored the relationship between pain and depression in two samples of patients with cancer: a) 96 subjects - 48 in the high pain group and 48 in the low pain group; and b) 35 patients with metastatic carcinoma of the breast. Prevalence of depression was found to be significantly higher in the high pain rather than in the low pain group.[29] Pain intensity was also found to correlate significantly with fatigue, vigor, and total mood disturbance. Pain frequency correlated significantly with fatigue, vigor, and depression.[29] Aass[30] investigated the prevalence of anxiety and depression in 716 cancer patients and found that the prevalence of depression was 9% with age or gender having no influence on the occurrence of depression .[30] The prevalence of depression increased with distant metastases, with the time period of less than one month from diagnosis, and was seen with a relapse or disease progression.[30]

Perceived Health Status

Physical and mental health and social and role functioning are important components of perceived health status.[31] Frequency and severity of pain, psychological distress, and fatigue influences a patient's perceived health status, QOL, and length of hospital stay.[32] Fatigue has been linked with impairment in cognitive functioning and impaired perception and thinking ability.[5] Lee, Letz, Taylor, Mitchell, and Woods,[33] in a study of women's responses to environmental demands, found that depression or anxiety were more significantly related to both fatigue and vitality than were external stresses. A patient's beliefs about her health status have been shown to be an important determinant of health outcomes.[34]

Methodology

Sample and Setting

This study used a descriptive, correlational design. A convenience sample of 127 women with

stage II, stage III, or stage IV breast cancer who had undergone mastectomy and completed adjuvant chemotherapy were recruited for the study. The setting was an urban National Cancer Institute designated comprehensive cancer center located in the Eastern United States. The study was approved by the Institutional Review Board prior to participant accrual. All participants were recruited by either the physician co-principal investigator or the oncology clinical nurse specialist co-investigator during a regularly scheduled Medical Oncology Outpatient Clinic visit. Written informed consent was obtained from each participant.

The subjects completed the questionnaires in a quiet, comfortable room located in the outpatient clinic. It took approximately one hour for the subjects to complete the questionnaires. The breast cancer clinical nurse specialist remained with the patient during this time.

Instrumentation

The Sociodemographic Form was used to collect demographic and clinical data.

Fatigue was measured using the Piper Fatigue Scale (PFS)[35] and the Fatigue Visual Analogue Scale (VAS). Use of the Piper Fatigue Scale is congruent with the conceptual framework of this study which recognizes that fatigue is a multidimensional symptom.[11] Piper (p. 485) [35] stated that in this model of fatigue, "...subjective perception was believed to be key to understanding how fatigue might vary between healthy and ill individuals". The PFS scale was designed to measure fatigue as a multidimensional phenomenon. Subjective dimensions include perceptions regarding the temporal, sensory, affective, and severity components of fatigue. The objective dimension includes signs of fatigue which could be validated by physiologic, biological, and behavioral means.The scale consists of 41 horizontal VAS items measuring four dimensions of subjective fatigue: a) the temporal dimension (5 items relating to timing, frequency, pattern, and duration of fatigue); b) the

intensity/severity dimension (12 items relating to severity, distress, and degrees of disruption in activities of daily living); c) the affective dimension (5 items relating to the emotional meaning of fatigue); and d) the sensory dimension (19 items relating to the physical, emotional, and mental symptoms of fatigue).[35]

Subjects using the PFS scale are asked to respond to items in terms of how they feel now. Anchors on the VAS vary depending on the item. Individual subscale scores are calculated by measuring each VAS item with a 100mm ruler from the left end to the subject's mark, summing all items within the subscale, then dividing the sum by the number of items on the subscale to obtain a mean value. A total fatigue score is calculated by summing the four scores and dividing by four. In a preliminary study by the principal investigator, Cronbach's alpha estimated for the 4 subscales in autotransplantation patients ranged from .83 to .98.

The Fatigue VAS is a 100mm vertical visual analogue scale anchored with "completely exhausted" and "no fatigue". The subject marks with a horizontal mark through the vertical line indicating the degree of fatigue which she is currently experiencing. Reliability and validity of the Fatigue VAS have been demonstrated through the VAS scales used on the Piper Fatigue Scale.

Pain was measured using the Painometer© (POM), which was designed to assess patients' overall pain intensity and intensity of the sensory and affective components of pain, as well as the quality of pain .[36] The Gate Control Theory of Pain[37] is the conceptual framework for this tool. The POM is a hard, white plastic tool which measures 8 inches long, 2 inches wide, and 1 inch thick. It is light weighted and is held easily by the subject. A list of 15 sensory and 11 affective pain descriptors is located on the front side of the POM and a 100mm VAS with a moveable marker (POM-VAS) is located on the back side of the POM. An intensity value (from a low of "1" to a high

of "5") is predetermined for each sensory and affective word located on the POM-WDS. A maximum score of 36 can be obtained for the sensory component of pain and of 34 for the affective component. A total score can be obtained by adding the sensory and affective scores. Test-retest reliability, concurrent validity, and construct validity have been demonstrated.[36] The Painometer® Questionnaire was used to record pain intensity, pain quality, pain locations, duration (whether the pain was continuous or periodic), and length of present pain episodes.

The Beck Depression Inventory (BDI) was used to measure depression in subjects. The BDI consists of 21 items that describe particular symptoms of depression .[38] Subjects respond to a Likert-type scale by rating each item 0 (no symptom) to 3 (severe or persistent presence of the symptom). Scores may range from 0 to 9 (normal), 10 to 15 (mild depression), 16 to 23 (moderate depression), and 24 to 63 (severe depression). The total possible score (range 0 to 63) is obtained by summing the 21 responses. Reliability and validity have been reported for the BDI.[38]

Perceived health status was measured by the Medical Outcomes Study Short-form General Health Survey (MOS-SF)[39]. This 20-item survey assesses physical functioning (6 items), role functioning (2 items), social functioning (1 item), mental health (5 items), health perception (5 items), and pain (1 item)[39]. Physical functioning refers to limitations in a variety of physical activities. Role and social functioning are defined as limitations related to health problems. Mental health is assessed in terms of both psychological distress and well-being. Health perception is assessed by the patients' perceptions of their own health in general, and pain refers to differences in physical comfort. The total health perception score is obtained by summing all of the mental health scales' scores for a possible score range of 0 to 91.[39] The Pain and Social Functioning subscales have a possible score range of 1 to 6. The Role Functioning subscale has a possible range of 0 to 6. The Physical Functioning

subscale has a possible score range of 1 to 18. The Mental Health subscale has a possible score range of 1 to 30, and the Health Perception subscale has a possible score range of 1 to 25.

Construct validity was demonstrated by showing that poor health was significantly greater ($p < .001$) in a patient sample than a general population sample regarding physical and role functioning, mental health , and health perceptions. Statistically significant ($p < .01$) correlations were found among all health measures. Cronbach's alpha estimated for the four multi-item scales ranged from .81 to .88. [39] In a preliminary study by the principal investigator, Cronbach's alpha for the MOS-SF in autotransplantation patients ranged from .58 to .98 for the subscales.

Data Analysis

Measures of central tendency (frequency, percent, mean, median, and standard deviation) were used to describe the sample and responses to the instruments. Correlations among multiple dimensions of fatigue and pain, depression and health status were analyzed using Pearson's product moment correlations and Spearman's Rho correlations, as appropriate. Hierarchial multiple linear regression techniques were used to determine the predictors of total health status and perceived health status.

Results

Sample Characteristics

The sample of 127 female subjects with breast cancer, ranging in age from 22 years to 60 years ($\underline{M} = 45 \pm 7.6$), was composed of 111 Caucasians (87%), 11 African Americans (9%), and 4 other minorities (3%) (Table 1). Most of the subjects were married (73%) and living with their spouse (72%), with an average yearly household income of equal to or over $50,000 (58 %). The sample was primarily Protestant (46%), college educated (53%), and employed (67%) in a

professional position (57%). All subjects had received previous surgery and adjuvant chemotherapy.

Fatigue

Ninety-one percent reported fatigue as measured by the Fatigue VAS. Subjects reported a mean total Fatigue VAS rating of 28 (SD = 25.5). The mean total Piper Fatigue Scale rating was 31.3 (SD = 20). Multiple dimensions of fatigue scores are presented in Table 2.

Pain

Forty-seven per cent of the participants reported pain as measured by the POM-VAS. All mean pain intensity scores for the subjects who experienced pain were low: affective pain intensity score was 1.72 (SD = 3.87); sensory pain intensity score was 2.34 (SD = 3.72); total pain intensity score was 4.05 (SD = 6.94); and overall pain intensity score was 8.4 (SD = 16.76) (Table 2). Although the mean pain scores for sensory, affective, total intensity and overall intensity were low, the range of reported scores was wide indicating that some subjects did experience moderate to severe pain intensity.

Depression

Fifty-four percent of the participants reported depression. The mean depression score was 10.92 (SD = 7.30) (Table 2). Depression ranged from mild (30%), to moderate (19%), to severe/high (5%), with 46% of the subjects reporting normal scores.

Health Status

Subjects reported a mean total perceived health status rating of 50.73 (SD = 10.79) out of a possible total rating range of 0 to 91 (Table 3). A high mean rating was reported for mental health ($\underline{M}$ = 21.95, SD = 4.59). A moderate mean rating was reported for pain ($\underline{M}$ = 4.19, SD = 1.27), social function ($\underline{M}$ = 4.74, SD = 1.36), and health perception ($\underline{M}$ = 15.10 , SD = 4.95). A low mean

rating was reported for physical functioning (M = 3.82, SD = 1.70). The lowest mean was reported for role functioning (M= .84, SD = .89).

The Influence of Fatigue, Pain, and Depression on Health Status

Correlations between pain, fatigue, depression, and health status are presented in Table 4. Significant correlations were observed between all variables except the following: fatigue temporal dimension and affective dimension and health status physical function; fatigue severity (VAS) and health status physical function; overall pain intensity and health status physical function; fatigue temporal dimension and health status role function; fatigue severity (VAS) and health status role function; fatigue temporal dimension and health status social dimension; overall pain intensity and fatigue temporal dimension.

The variables of interest (fatigue, pain, and depression) were all significantly correlated to total health status. Variance in health status was determined after controlling for demographic variables. Depression ($B = -.94$, $\beta = -.65$, $p < .001$) and sensory pain ($B = -.53$, $\beta = -.19$, $p < .01$) accounted for 64% (adjusted $R^2 = .60$, F statistic = 15.37) of the variance in total health status. Depression ($B = -.94$, $\beta = -.65$, $p < .001$) and affective pain ($B = -.45$, $\beta = -.17$, $p < .05$), accounted for 63% (adjusted $R^2 = .59$, F statistic = 14.90) of the variance in the total health status. Fatigue ($B = .04$, $\beta = -.19$, $p < .05$) and depression ($B = -.27$, $\beta = -.41$, $p < .001$) accounted for 42% (adjusted $R^2 = .36$, F statistic = 6.46) of the variance in the perception of health status.

Discussion

The sample was composed of a select group of primarily highly educated, married Caucasian patients, who were employed in professional occupations with average yearly incomes greater than $50,000. Although participants overall exhibited low to moderate levels of pain, depression, and

fatigue, a large number of women reported some symptoms and usually experienced multiple symptoms.

Almost all (91%) of women reported feelings of fatigue which was highly significantly correlated with overall total health status. The dimensions of fatigue which most highly correlated with total health status were the intensity/severity and sensory dimensions. Not surprisingly, these are the dimensions that encompass the degrees of disruption in activities of daily living and the physical, emotional, and mental symptoms of fatigue which signal a reduction in health status. Participants rated their pain from 0 to 4.4 on a 10cm VAS. Total pain scores were inversely related to health status. Interestingly, pain was significant, but only slightly correlated with depression.

Depression was a frequently cited symptom of more than half of the respondents with almost a quarter of the subjects reporting moderate to high levels of depression. Depression was highly correlated with fatigue particularly the intensity/severity and sensory dimensions of fatigue. Consequently, fatigue's effect on an individual's inability to carry out various daily activities is highly associated with depression. Research conducted by Aass et al.[30] determined that fatigue increased the odds of the occurance of depression. Depression was also highly negatively correlated with total health status, specifically with the social functioning and perception of health status domains. Other investigators have also reported that long after a patient has undergone mastectomy followed by chemotherapy, fatigue, pain, and depression continue to alter health perception[40]. Thus the multiplicity of symptoms may have important consequences for health outcomes post-chemotherapy. Previous studies using instruments that incorporated constructs of both depression and fatigue were limited in their ability to discriminate between the two symptoms.[8] Depression and pain accounted for a large amount of the variance in the regression model and were most predictive of total health

status. The results of this study suggest that fatigue is associated with total health status through perception of health status and the multicollinearity of fatigue and depression resulted in a decrease in variance of total health status.

The findings are limited because of the small numbers of minority patients, as well as the select sample of high socioeconomic status women who were recruited. This study should be replicated to determine if differences exist in the manifestation of the fatigue-pain-depression triad in other groups to increase the generalizability of findings. Future research could also be designed to study whether preexisting symptoms experienced by women scheduled for adjuvant chemotherapy are predictors of increased severity of fatigue, pain, and depression post-chemotherapy. In addition, further clarification is needed to determine if preexisting symptoms act as antecedental variables and thus moderate succeeding symptoms and related distress post-chemotherapy. These underlying symptoms may contribute to even greater symptom severity in future breast cancer treatments.

Clinical Implications

Results demonstrated that although participants did not manifest extreme levels of fatigue, pain, or depression, they were far from being symptom free, and these symptoms had a large impact on their health. The results of this study should serve as an important reminder that the majority of women undergoing mastectomy followed by adjuvant chemotherapy continue to experience symptoms long after treatment has ended and may not receive any further validation of their symptom experience.

Although most patients reported low to moderate symptom severity levels, the presence of fatigue, pain, and depression in some breast cancer patients requires vigilant nursing assessment and intervention. Nursing interventions which instruct patients in symptom management strategies such

as the use of cognitive restructuring, exercise, and relaxation with guided imagery are congruent with this viewpoint. For example, interventions that change how breast cancer patients perceive their health status may reduce symptom severity and positively affect their total health status. Self-care procedures, such as the use of a comprehensive coping strategy program, may prove to be an efficient and effective means of alleviating symptoms.

Researchers investigating the symptom experience and health outcomes have advocated assessing the patient's perspective to gain a deeper understanding of the symptom perception, evaluation, and response to symptoms.[41] Evidence that a subject's perception of her health status is highly correlated with her actual health status supports this approach. Patients are the key source of information about their symptom experience in relation to their overall health.

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Table 1. Demographic Characteristics of the Sample (n = 127)

Demographic Characteristics	n	%
Gender		
Female		100
Age		
Mean	45	
SD	7.6	
Range	22-60	
Ethnicity		
Caucasian	111	87.4
African-American	11	8.7
Other Minorities	4	3.1
Marital Status		
Married	93	73.2
Single	18	14.2
Divorced	14	11
Separated	1	.8
Education Completed		
High School	23	18.1
Some College	35	27.6
College Graduate	39	30.7
Graduate Degree	28	22
Religion		
Catholic	31	24.4
Protestant	59	46.5
Jewish	9	7.1
Other	20	15.1
None	4	3.1
Patient Lives With		
Spouse	91	71.7
Other	14	11
Self	20	15.7
Average Yearly Income		
<$50,000.	39	30.7
≥ $50,000.	74	58.3
Occupation		
Professional	72	56.7
Non-professional	42	33.1
Work Status		
Employed	85	66.9
Unemployed	37	29.1

Note: Some patients chose not to answer all questions. Missing data excluded for percentage computation where applicable.

Table 2. Mean Fatigue, Pain, and Depression Ratings (n = 127)

	Mean	SD	Range
Fatigue			
Temporal Dimension	35.20	35.59	0 to 79
Intensity/Severity Dimension	20.76	19.77	0 to 74
Affective Dimension	34.38	25.26	0 to 92
Sensory Dimension	36.52	21.06	0 to 88
Total	31.26	19.98	0 to 87
VAS	28.25	25.46	0 to 97
Pain			
Affective Dimension	1.71	3.87	0 to 28
Sensory Dimension	2.34	3.72	0 to 22
Total	4.05	6.94	0 to 44
VAS	8.43	16.76	0 to 100
Depression	10.92	7.30	0 to 37

Table 3. Mean Health Status Ratings (n = 127)

Items on MOS-SF	Mean	SD	Range
Health Status			
Pain	4.20	1.27	1 to 6
Physical Functioning	3.82	1.70	0 to 6
Role Functioning	.84	.90	0 to 2
Social Functioning	4.74	1.36	1 to 6
Mental Health	21.95	4.59	8 to 30
Health Perception	15.11	4.95	5 to 25
Total	50.73	10.79	18 to 72

Table 4. Correlations Between Depression, Multiple Dimensions of Fatigue and Pain, and Health Status (n =127)

	HS Total	Physical Func	Role Func	Social Func	Mental Health	Perception	Pain	Fatigue Total	Fatigue Temp	Fatigue I/S	Fatigue Affective	Fatigue Sensory	Fatigue VAS	Pain Total	Pain Sen	Pain Aff	Pain VAS	Depression
Health Status Total	1																	
Physical Function	.54***	1																
Role Function	.61***	.67***	1															
Social Function	.73***	.46***	.54***	1														
Mental Health	.75***	.18*	.27*	.44***	1													
Perception	.84***	.31***	.41***	.50***	.42***	1												
Pain	.58***	.41***	.41***	.58***	.21*	.43***	1											
Fatigue Total	-.59***	-.30***	-.35***	-.40***	-.48***	-.49***	-.35***	1										
Temporal	-.30*	-.11	-.04	-.14	-.23*	-.33***	-.17	.74***	1									
Intensity/Severity	-.61***	-.34***	-.46***	-.51***	-.47***	-.45***	-.40***	.81***	.39***	1								
Affective	-.42***	-.17	-.30**	-.29 **	-.32***	-.34***	-.34***	.79***	.29**	.62***	1							
Sensory	-.60***	-.40***	-.41***	-.38***	.56***	-.42***	-.24**	.82***	.36***	.70***	.67***	1						
Fatigue VAS	-.33***	-.11	-.23	-.31***	-.18*	-.33***	.27**	.53***	.33***	.54***	.42***	.45***	1					
Pain Total	-.38***	-.26**	-.22*	-.39***	-.21*	-.30**	-.44***	.33***	.33***	.27**	.28**	.33***	.33***	1				
Sensory Pain	-.37***	-.25**	-.20*	-.36***	-.20*	-.28**	-.45***	.32***	.20*	.26**	.24**	.31***	.27**	.91***	1			
Affective Pain	-.34***	-.23**	-.20*	-.35***	-.18*	-.26**	-.36***	.28***	.28**	.24**	.26**	.30**	.33***	.92***	.67***	1		
Pain VAS	-.32***	-.13	-.19*	-.32***	-.31**	-.19*	-.26**	.34***	.15	.32***	.30**	.32***	.30*	.25**	.23*	.23*	1	
Depression	-.73***	-.32***	-.42***	-.59***	-.69***	-.51***	-.34***	.58***	.19*	.65***	.48***	.66***	.34***	.23*	.19*	.22*	.25**	1

*p <.05 **p < .01 ***p < .001

Appendix C

Pain, Psychological Distress, Health Status, and Coping in Breast Cancer Patients Scheduled for Autologous Bone Marrow Transplantation

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Purpose/Objectives: The purpose of this study was to describe pain, psychological distress, health status, and coping experienced by breast cancer patients who were scheduled for autologous bone marrow transplantation (ABMT). Strength and direction of relationships among pain, psychological distress, health status, and coping were explored. The percentage of variance within the concept of health status which was explained by age, pain, psychological distress, and coping (ability to control pain, use of positive coping statements, and catastrophizing) was also examined.

Design: A descriptive, correlational design was used.

Setting: The setting was an urban, National Cancer Institute designated Comprehensive Cancer Center located in the eastern United States.

Sample: A convenience sample of 83 female breast cancer patients scheduled for ABMT was used. The population age ranged from 22 to 59 years ($\underline{M}$ = 44.47 years) and was composed of 72 Caucasian (88 %), 6 African American (7 %), and 4 other minorities (5 %) patients.

Methods: The data were collected by an oncology clinical nurse specialist in the outpatient medical oncology clinic during a regularly scheduled visit approximately 20 days pre-hospitalization for intensive chemotherapy and ABMT. Sociodemographic data were collected using the Patient Demographic Data Form. The following self-report instruments were used: Gaston-Johansson Painometer®; State-Trait Anxiety Inventory; Beck Depression Inventory; MOS Short-form General Health Survey; and Coping Strategies Questionnaire.

Main Research Variables: Pain, psychological distress, health status, and coping.

Findings: The sample characteristics consisted of a select group of highly educated, primarily Caucasian patients, who were married, living with their spouse, and employed in professional occupations with yearly incomes of greater than $50,000. The subjects experienced low pain

intensity. However, the range of reported pain intensity ratings was wide, indicating that some patients experienced at least moderate pain intensity. Pain locations were varied; pain was experienced primarily in the vagina, chest, shoulder, and arm and described most frequently as aching, sore, dull, annoying, tiring, nagging, and troublesome. Participants reported primarily mild depression and mild state anxiety. However the range of depression and state anxiety scores was wide, indicating that some subjects experienced severe depression and severe anxiety. Coping strategies used most frequently to deal with pain included use of positive coping statements, diverting attention, praying and hoping, increasing activity level, ability to control pain, and ability to decrease pain. Subjects reported moderate total health status and a low role functioning. High, significant positive correlations were seen between state anxiety and depression, and physical functioning and role functioning. High, significant, negative correlations were seen between state anxiety and mental health, depression and total health status, and depression and mental health. Sixty-five percent of the variance in health status was explained by sensory pain, depression, and catastrophizing.

Conclusions: Breast cancer patients scheduled for ABMT may experience pain, psychological distress, and alterations in coping and perceived health status during the pre-hospitalization for ABMT time period. Total pain intensity, affective pain, depression, and catastrophizing appear to be important variables related to the perceived health status of the patient.

Implications for Nursing Practice: Oncology nurses need to include assessment of pain, psychological distress, health status, and coping in their routine patient assessment prior to ABMT. These patients may experience difficulty in coping not only with the breast cancer diagnosis, but also with previous surgical treatment and related pain, as well as anticipatory psychological distress

regarding the future scheduled intensive chemotherapy and ABMT process. Health care providers need to be cognizant of these potential patient psychological and physiological problems to provide appropriate care and make necessary referrals to members of the multidiciplinary health care team. Future nursing research should be directed toward the testing and implementation of comprehensive coping strategy interventions to promote the use of positive coping strategies to decrease pain, anxiety, and depression.

Introduction

The American Cancer Society estimates 178,700 new cases of female breast cancer in the United States in 1998, and that 43, 500 women will die from this disease (Landis, Murray, Bolden, & Wingo, 1998). Although the 5-year survival rate for breast cancer that is diagnosed at a local stage is currently 97%, this rate decreases to 20% when the cancer is diagnosed with distant metastases (U. S. Department of Health and Human Services, 1997). Clearly, innovative treatment strategies are needed to increase these survival rates. One such treatment modality is the use of autologous bone marrow transplantation (ABMT) for women with metastatic or high-risk, early stage breast cancer. Autologous BMT uses high dose chemotherapy to achieve maximum tumoricidal dose followed by bone marrow rescue with reinfusion of the patient's own cryopreserved bone marrow cells. This treatment modality has become wide-spread (Whedon, 1996); more than 5,000 ABMTs are performed annually worldwide (Buschel, Leum, & Randolph, 1996).

The purpose of this study was to describe and examine relationships among pain, psychological distress, perceived health status, and coping in breast cancer ABMT patients during the preadmission phase. The relationships were examined among pain, psychological distress, perceived health status, and coping. The percentage of variance within perceived health status which can be explained by pain, psychological distress, and coping (ability to control pain, use of positive coping statements, and catastrophizing) was also investigated.

Literature Review

The literature presents research regarding the pain, psychological distress, and coping experienced by these patients during and after the ABMT hospitalization period (Ford & Ballard, 1988; Gardner, August, & Githens, 1977; Gaston-Johansson, Franco, & Zimmerman, 1992; Hill et al., 1990;

Jenkins & Roberts, 1991). However, there is a paucity of research conducted exploring these variables during the pre-hospitalization period. Meyers et al. (1994) explored the cognitive and emotional functioning of 61 adult patients before, during, and after BMT. Results demonstrated nearly 40% of the sample experienced significant anxiety pre-BMT (Meyers et al). Pre-hospitalization data are extremely significant because a patient's anticipatory response to the ABMT procedures and associated intensive chemotherapy may be an important predictor of subsequent or long term quality of life (QOL) (Gaston-Johansson & Foxall, 1996) and the development of neurobehavioral disorders (Meyers et al.).

Pain

Pain has been shown to be a significant problem for a large number of stage I and stage II breast cancer patients (Arathuzik, 1991; Miaskowski & Dibble, 1995a; Miaskowski & Dibble, 1995b). Pain may be acute, as experienced prediagnosis, following lumpectomy or mastectomy and axillary node dissection, or may be chronic and long-term in nature (Gorrell, d'Angelo, & Bagley, 1988). Treatment-related breast pain from surgery and chemotherapy is related to breakdown of the skin integrity. This treatment-related pain has been characterized as irritating (Gorrell, d'Angelo, & Bagley), constricting, burning, or throbbing sensations localized to the posterior arm, axilla, and anterior chest wall (Assa, 1974; Eliott & Foley, 1989; Johnson, 1994; Wood, 1978). Only one published study to date could be found that examined the pain experienced by breast cancer patients and its effects on their lives in the outpatient setting (Miaskowski & Dibble, 1995a). The study results found that 47% of breast cancer patients receiving treatment in the outpatient setting reported cancer-related pain. The majority of patients in this group were found to have treatment-related pain from post-surgical neuropathic pain syndrome (56%) and cancer-related pain from bone metastasis

(26%). Patients rated their pain as moderate to severe on a daily basis.

Patients who experience cancer pain are found to have significantly more depression, anxiety, and decreased QOL scores than pain-free patients (Ferrell, Dow, Leigh, Ly, & Gulamsekaram, 1995; Ferrell & Funk, 1995; Miaskowski & Dibble, 1995a). Many patients suffering from chemotherapy related pain in the outpatient settings have reported using non-pharmacologic approaches such as relaxation, massage, and imagery to reduce discomfort. Pilot studies by Arathuzik (1994) found that educating breast cancer patients in relaxation techniques and cognitive coping skills was effective in decreasing pain. These non-pharmacologic approaches used separately have proven to be effective in relieving pain in both breast and lung cancer patients (Arathuzik, 1994; Ferrell-Torry & Glick, 1993; Wilkie, 1990; Wilkie, 1991). However, these approaches have not been evaluated in combination in a randomized controlled clinical trial (Arathuzik; Ferrell-Torry, & Glick; Wilkie 1990; Wilkie, 1991).

Psychological Distress and Coping

Six psychosocial stages corresponding to the medical management of BMT have been identified (Brown & Kelly, 1984; Haberman, 1988). The initial two stages--making the decision to undergo a BMT and the preadmission stage-- are contextually appropriate for this study. The decision-making stage represents a major turning point in the patient's life (Haberman). Numerous factors influence the patient's decision to undergo a BMT. The cost/benefit ratio of possibly achieving increased survival time versus potential acute and chronic negative sequelae is a major factor (Haberman). Uncertainties may linger after this decision-making stage and may be present during the pre-admission stage and other stages. The preadmission stage presents the breast cancer patient with unique psychological demands and concerns. The patient may experience stress from

numerous sources such as recent breast cancer surgery, knowledge of a life-threatening diagnosis, and uncertainty regarding the future ABMT treatment process and outcome (Jenkins, Limington, & Whittaker, 1991).

Anxiety and depression are common responses to the diagnosis of and treatment for breast cancer (Gobel & Donovan, 1987; Maraste, Brandt, Olsson, & Ryde-Brandt, 1992; Schain, d'Angelo, Dunn, Lichter, & Pierce, 1993). Elevated levels of depression and anxiety may persist in a minority of breast cancer patients even years after the diagnosis (Spiegel, 1997). Adjuvant chemotherapy represents a prolonged threat to a patient's mortality and functioning leading to additional psychological distress after breast surgery. One study indicated that 14% of patients who underwent adjuvant chemotherapy after breast-conserving surgeries and mastectomies experienced severe anxiety (Maraste et al., 1992). Coscarelli-Shag et al. (1993) identified the following major sources of psychological distress for breast cancer patients at one month post diagnosis: a) anxiousness while waiting for test results and having to undergo additional diagnostic tests; b) worries over whether the cancer was progressing; c) concern about ability to take care of self; and d) concern about how the family would manage if the patient died. Assessing patients' anxiety and depression during the pre-admission period is of paramount importance to provide appropriate interventions and because it is critical that the ABMT patients adhere to the strict treatment protocol schedule.

Coping behaviors are direct attempts to manage pain (Arathuzik, 1991). Although investigators have described coping strategies for pain, few have described the nature of this coping with pain (Arathuzik, 1991; Copp, 1990; Graffam & Johnson, 1987). Gaston-Johansson et al. (1992) reported that patients undergoing ABMT used inadequate coping strategies and stated that they experienced little ability to control or decrease their pain. Numerous challenges to coping exist: the change to

outpatient status; potential geographical dislocation; and the preparation of significant others for the possibility of morbidity and death. Behavioral issues such as decreased pain tolerance and pain related to procedures, disease and/or prior treatment may be evident (Syrjala, 1995). Coping issues related to decision-making regarding treatment and access to and use of psychological supports may be present. Psychological responses, such as distress, may be operational (Syrjala).

Perceived Health Status

Frequency and severity of pain, psychological distress, and fatigue influences a patient's perceived health status, QOL, and length of hospital stay (Chielens & Herrick, 1990). A patient's beliefs about his health status have been shown to be an important determinant of health outcomes (Wolcott, Wellisch, Fawzy, & Landsverk, 1986). The health status of ABMT patients varies. Some breast cancer ABMT patients leave the hospital within three weeks, while others stay 2 to 3 months. About 35% of patients utilize emergency room services and about 15 to 50% require one or more rehospitalizations (Chielens & Herrick).

Conceptual Framework

The Gate-Control Theory of Pain developed by Melzack and Wall (1965) and the Stress, Coping, and Adaptation Paradigm formulated by Lazarus and Folkman (1984) provided the theoretical framework for this study. Pain is defined as a multi-dimensional sensory and affective experience associated with discomfort (International Association for the Study of Pain, 1979). According to the Gate-Control Theory of Pain, the central system located in the brain can be stimulated by cognitive processes such as past experiences, anxiety, anticipation, and attention, which open the gating mechanism permitting the transmission of nociceptive impulses to the brain (Melzack and Wall).

Coping is defined as constantly changing cognitive and behavioral efforts used to manage specific

external and/or internal demands that are appraised as taxing or exceeding the resources of a person (Lazarus & Folkman, 1984). Positive coping strategies refer to internal thoughts and behaviors people use to manage their pain, or their emotional reactions to the pain, and to reduce emotional distress. Catastrophizing, a negative coping strategy, is defined as a method of cognitive coping characterized by negative self-statements and thoughts about the future (Keefe et al., 1987; Keefe, Brown, Wallston, & Caldwell, 1989).

Research Objectives

The study had the following research objectives:

1. Describe pain and psychological distress in breast cancer patients during the pre-hospitalization for ABMT time period.
2. Describe the health status of breast cancer patients during the pre-hospitalization for ABMT time period.
3. Examine the relationships among pain, psychological distress, catastrophizing, coping, and perceived health status in breast cancer patients during the pre-hospitalization for ABMT time period.
4. Describe the percentage of variance within the concept of health status which was explained by pain, psychological distress, and coping (ability to control pain, use of positive coping statements, and catastrophizing).

Methods

Design

The study used a descriptive, correlational design.

Sample

A convenience sample of 83 women with stage II, stage III, or stage IV breast cancer scheduled for ABMT was recruited for the study.

Setting

The setting was an urban National Cancer Institute designated comprehensive cancer center located in the eastern United States.

Instruments

The **Sociodemographic Questionnaire** included the following information: age; gender; race/ethnicity; marital status; educational level; religion; patient living arrangements; average yearly household income; occupation; work status; and household income; and breast cancer stage.

Pain was measured using the **Painometer®** (POM), which was designed to assess patients' overall pain intensity and intensity of the sensory and affective components of pain, as well as the quality of pain (Gaston-Johansson, 1996). The POM is a hard, white plastic tool which measures 8 inches long, 2 inches wide, and 1 inch thick. It is light weighted and is held easily by the subject. A list of 15 sensory and 11 affective pain descriptors is located on the front side of the POM and a 100mm visual analogue scale (VAS) with a moveable marker (POM-VAS) is located on the back side of the POM. An intensity value (from a low of "1" to a high of "5") is predetermined for each sensory and affective word located on the POM-WDS. A maximum score of 36 can be obtained for the sensory component of pain and of 34 for the affective component. A total score can be obtained

by adding the sensory and affective scores. High correlations were found between the initial and the repeat pain intensity ratings on the POM-VAS ($r = 0.88$, $p < 0.001$) and the POM-WDS ($r = 0.84$, $p < 0.001$) (test-retest reliability). Correlations between the POM-WDS and the McGill Pain Questionnaire ($r = 0.69$, $p < 0.001$) and POM-VAS ($r = 0.85$, $p < 0.001$) supported the concurrent validity of the POM-WDS. Construct validity was also supported for the POM by showing that pain scores decreased significantly from POM-WDS ($t = 5.53$, $p < 0.001$), and POM-VAS ($t = 6.18$, $p < 0.001$) after the treatment with pain medication. The POM took about 2 minutes to complete. The **Painometer® Questionnaire** was used to record pain intensity, pain quality, pain locations, duration (whether the pain was continuous or periodic), and length of present pain episodes.

The **Beck Depression Inventory** (BDI) was used to measure depression in subjects. The BDI consists of 21 items that describe particular symptoms of depression (Beck & Steer, 1987). Subjects respond to a Likert-type scale by rating each item 0 (no symptom) to 3 (severe or persistent presence of the symptom). Scores may range from 0 to 9 (normal), 10 to 15 (mild depression), 16 to 23 (moderate depression), and 24 to 63 (severe depression). The total possible score (range 0 to 63) is obtained by summing the 21 responses. Reliability and validity have been reported for the BDI.

The **State-Trait Anxiety Inventory** (STAI) was used to measure anxiety (Spielberger, 1983). The STAI consists of two separate self-report scales for measuring state and trait anxiety (Spielberger). State anxiety is a transitory emotional response to a stressful situation. Trait anxiety reflects a stable predisposition to anxiety as determined by a personality pattern. Each scale consists of 20 statements as related to emotions and respondents rate themselves in relationship to each statement on a Likert-type scale from 1 to 4 (1 = "not at all", 2 = "somewhat", 3 = "moderately so", and 4 = "very much so"). The total score is the sum of all 20 responses and ranges from a minimum

score of 20 to 39 (low anxiety), 40 to 59 (moderate anxiety), to a maximum score of 60 to 80 (high anxiety). Scores are reported to be considerably higher under stressful conditions than under normal conditions (Spielberger). Reliability and validity have been demonstrated for this instrument (Spielberger).

The **Coping Strategy Questionnaire** (CSQ) developed by Keefe et al. (1987) was used to assess the patient's use of coping strategies. The categories of coping strategies assessed by this measure include: a) diverting attention; b) reinterpreting pain sensations; c) ignoring pain sensations; d) praying and hoping; e) catastrophizing; and f) increasing activity level. For each category of coping strategies there are 6 items on the CSQ with scores ranging from 0 to 36. Each item is rated on a 7 point scale to indicate how often that strategy is used to cope with pain (0 = "never", 3 = "sometimes", and 6 = "always"). Reliability of the CSQ has been demonstrated with alpha coefficients ranging from .71 to .85. Cronbach's alpha ranged from .71 to .88 in chemotherapy patients. The CSQ also includes 2 items which measure overall effectiveness of those strategies used by asking the subjects to rate on a 7-point scale (with scores ranging from 0 to 6) how much control they have over the pain, and how much they are able to decrease their pain (Keefe et al., 1990). Construct validity has been demonstrated by factor analysis (Keefe et al., 1990; Carey & Burish, 1987).

Perceived health status was measured by the **Medical Outcomes Study Short-form General Health Survey** (MOS-SF) (Stewart, Hays, & Ware, 1988). This 20-item survey assesses physical functioning (6 items), role functioning (2 items), social functioning (1 item), mental health (5 items), health perception (5 items), and pain (1 item) (Stewart et al., 1988). Physical functioning refers to limitations in a variety of physical activities. Role and social functioning are defined as limitations

related to health problems. Mental health is assessed in terms of both psychological distress and well-being. Health perception is assessed by the patients' perceptions of their own health in general, and pain refers to differences in physical comfort. The total health perception score is obtained by summing all of the mental health scales' scores (Stewart et al., 1988) for a possible score range of 0 to 91. The Pain and Social Functioning subscales have a possible score range of 1 to 6. The Role Functioning subscale has a possible range of 0 to 6. The Physical Functioning subscale has a possible score range of 1 to 18. The Mental Health subscale has a possible score range of 1 to 30, and the Health Perception subscale has a possible score range of 1 to 25.

Construct validity was demonstrated by showing that poor health was significantly greater ($p < .001$) in a patient sample than a general population sample regarding physical and role functioning, mental health and health perceptions. Statistically significant ($p < .01$) correlations were found among all health measures. Cronbach's alpha estimated for the four multi-item scales ranged from .81 to .88 (Stewart et al., 1988). In a preliminary study by the PI, Cronbach's alpha for the MOS-SF in ABMT patients ranged from .58 to .98 for the subscales.

Procedure

The study was approved by the Institutional Review Board prior to participant accrual. All participants were recruited by either the physician co-investigator or the oncology clinical nurse specialist co-investigator during a regularly scheduled pre-ABMT Medical Oncology Outpatient Clinic visit. All participants had been accepted into the ABMT program prior to the invitation to participate in this study. Written informed consent was obtained from each participant.

The subjects completed the questionnaires in a quiet, comfortable room located in the outpatient clinic. The breast cancer clinical nurse specialist remained with the patient during this time.

Occasionally, subjects requested to complete the questionnaires at home It took approximately one hour for the subjects to complete the questionnaires.

Data analysis

Descriptive statistics (frequency, percent, mean, mode, and standard deviation) were used to describe the sample and responses to the instruments. Correlations among pain intensity and quality, psychological distress, catastrophizing, coping, and perceived health status were examined using Pearson product moment and Spearman's Rho correlations as appropriate. Hierarchial multiple linear regression techniques were used to determine the best fit model which explained the maximum variance of total health status, within the context of the study. Covariates in the model included age, pain, psychological distress, and coping (ability to control pain, use of positive coping statements, and catastophizing).

Results

Sample Characteristics

The sample of 83 female subjects, ranging in age from 22 years to 59 years ($\underline{M} = 44.47 \pm 7.29$), was composed of 72 Caucasians (88%), 6 African Americans (7%), and 4 other minorities (5%) ABMT patients (Table 1). Most of the subjects were married (74%) and living with their spouse (73%), with an average yearly household income of over $50,000 (68%). The sample was primarily Protestant (51%), college educated (52%), and employed (72%) in a professional position (62%). All subjects had received previous chemotherapy and surgery.

Pain

Fifty-four % of the subjects experienced no pain. All mean pain intensity scores for the subjects who experienced pain were low: affective pain intensity score was 3.45 (SD = 4.14; range = 1 to

14); sensory pain intensity score was 4.47 (SD = 3.67, range = 1 to 20); total intensity score mean was 6.92 (SD = 6.86, range = 1 to 44); and POM-VAS overall pain intensity score was 7.47 ± 13.99 (Table 2). Although, the mean pain scores were low for sensory, affective, overall intensity, as well as for the POM-VAS, the range of reported scores was wide indicating that some subjects did experience moderate pain intensity.

The words chosen most frequently using the POM-WDS to describe the sensory quality of pain were aching (25%), sore (24%), and dull (13%), and the words chosen most frequently to describe the affective quality of pain were annoying (26%), tiring (17%), nagging (10%), and troublesome (10%) (Table 3). Sensory words not chosen using the POM-WDS were splitting and searing and the affective word not chosen was sickening. Locations of pain experienced by the study participants were primarily in the vagina (19%), chest (14%), shoulder (13%), and arm (10%) (Table 4). Other varied locations, each noted by only 1 to 5 subjects, were the neck, abdomen, breast, joint/hand, mouth, head (ache), rectum, eyes, hips, foot, and generalized.

Psychological Distress

The participants reported anxiety and depression. Anxiety ranged from mild (49%), moderate (24%) to severe/high (26%). Depression ranged from mild (36%), to moderate (17%), to severe/high (7%), with 40% of the subjects reporting normal scores. The mean state anxiety score was 41.43 (SD = 12.67, range = 20 to 67) and the mean depression score was 11.66 (SD = 7.73, range = 0 to 37).

Cognitive Coping Strategies

The subjects used a variety of coping strategies to cope with pain (Table 5). Positive coping strategies such as coping statements ($\underline{M}$ = 22.15, SD = 6.19, range = 7 to 36), praying and hoping,

(M = 19.31, SD = 8.23, range = 2 to 35) and diverting attention (M = 17.08, SD = 7.66, range = 1 to 34) were used frequently. Catastrophizing, a negative coping strategy, was used less frequently (M = 6.22, SD = 5.87, range = 0 to 26). Overall effectiveness of the coping strategies results demonstrated that the participants experienced ability to control pain and ability to decrease pain.

Health Status

Subjects reported a mean total perceived health status rating of 50.30 (SD = 10.67, range = 18 to 72), out of a possible total rating range of 0 to 91. A high mean rating was reported for mental health (M = 22.10, SD = 4.5, range = 8 to 29). A moderate mean rating was reported for pain (M = 4.11, SD = 1.28, range = 1 to 6), social function (M = 4.73, SD = 1.44, range = 1 to 6), and health perception (M = 14.66, SD = 4.98, range = 5 to 25). The lowest mean was reported for role functioning (M= .79, SD = .87, range = 0 to 2). The distribution of total health scores is presented in Figure 1.

Correlations Between Pain and Selected Variables

Correlations between pain, anxiety, depression, catastrophizing, coping, and health status are presented in Table 6. Significant correlations were observed between the following variables: state anxiety and depression (.61, $p < .001$); and physical functioning and role functioning (.65, $p < .001$). Significant, negative correlations were seen between state anxiety and mental health (- .66, $p < .001$); depression and total health status (- .73, $p < .001$); and depression and mental health (- .71, $p < .001$).

The variables of interest (pain, anxiety, depression, ability to control pain, and catastrophizing) were all significantly correlated to total health status. Bivariate correlation co-efficients of these variables with total health status ranged from r = .33 (pain, $p < .01$) to r = .73 (depression, $p <$

.001). Regression results from the final model explained an overall variance of 65% (R^2 = .65, F statistic = 22.48 ($p < .05$) of the total health status based on the covariables in the final model. Statistically significant variables were affective pain ($\beta = -3.36$, $p < .05$), depression ($\beta = .73$, $p < .001$), and catastrophizing ($\beta = .36$, $p < .05$).

Discussion

The sample characteristics describe a select group of primarily highly educated Caucasian ABMT patients, who were married and living with their spouse, and employed in professional occupations with average yearly incomes greater than $50,000. All subjects had received surgery and chemotherapy prior to the planned ABMT. The low grade pain intensity and pain locations chosen of chest, shoulder, and arm and the pain descriptors of dull, sore, and aching may be related to previous breast cancer surgery (lumpectomy or mastectomy), or a previously placed or removed central venous catheter used for the prior chemotherapy. It is interesting to note that this sample of patients experienced pain before any invasive procedures related to the scheduled ABMT were performed, such as central line placement or bone marrow aspiration. Also of interest is the vaginal pain experienced. This may be related to chemotherapy-induced mucositis or atrophic vaginitis. The continuous nature of low intensity pain can be very tiring and debilitating for the patient.

Psychological distress was evident through the reporting of mild through severe depression and state anxiety. This fact demonstrates the necessity of screening for anxiety and depression in this population before admission for the ABMT. Positive coping strategies used to cope with pain were chosen by the majority of the subjects. However, the use of catastrophizing was present. Pre-admission data are important as potential prognosticators of long-term QOL (Gaston-Johansson & Foxall, 1996) and future neurobehavioral disorders (Meyers et al., 1994). Assessing patients' anxiety,

depression, and use of catastrophizing during the pre-admission period is also of paramount importance to provide appropriate interventions and because it is critical that the ABMT patients adhere to the strict treatment protocol schedule. The subjects reported a moderate total perceived health status. However, the range of scores was very wide with some subjects reporting very low total health status scores. The low mean rating for role functioning may be related to the change from a previously perceived role to the status of ambulatory care breast cancer patient awaiting ABMT. The significant, negative correlations between state anxiety and mental health, depression and total health status, and depression and mental health, and the significant, positive correlation between state anxiety and depression, as well as the variances in total health status explained by pain, state anxiety, and depression, demonstrate the importance of the timely assessment and treatment of these components of psychological distress.

Implications

Nursing Practice

Breast cancer patients scheduled for ABMT may experience pain, psychological distress, and alterations in coping during the pre-hospitalization period. These patients may experience difficulty in coping not only with the breast cancer diagnosis, but also with recent surgical treatment, and the anticipatory anxiety regarding the future scheduled intensive chemotherapy and ABMT process. The preadmission stage presents the breast cancer patient with unique psychological demands and concerns. Oncology nurses need to be cognizant of these potential complex psychological and physiological challenges to make appropriate assessments, perform effective nursing care, and make necessary referrals. The fast-paced ambulatory care environment in which many patients are seen pre-ABMT necessitates that oncology nurses perform very focused patient assessments. Nursing

assessments for anxiety, depression, and alteration in health status and coping should be a routine part of this pre-ABMT patient assessment. The U. S. economically driven trend toward earlier discharge for the BMT population makes this early assessment critical. Also some BMTs are now performed in a modified outpatient setting. Many ABMT patients are currently expected to achieve effective self-care skills during a stressful time period. Interventions to decrease anxiety, depression, and alterations in health status and coping may prevent the ABMT patient from becoming overwhelmed later in the ABMT treatment process and after discharge.

Nursing Research

Nursing research regarding interventions using findings from this and other relevant research targeted at the specific needs of breast cancer ABMT patients during the pre-hospitalization period regarding pain, psychological distress, and alterations in coping and health status is needed. Cognitive restructuring to change perception of pain and psychological distress, and decrease the use of catastrophizing, may be a useful component of this intervention. Nursing research is also needed regarding the etiology of pain in the breast cancer ABMT population. The findings presented here regarding vaginal pain in breast cancer ABMT patients are of interest within the context of sensitivity of mucosa to chemotherapy effects.

Research also needs to be directed toward discovering the reasons for the very low role perception. This role perception may become very important to the patient's ability to cope with the physiological and psychological challenges engendered by the ABMT treatment process.

Recruitment of increased numbers of minority patients into nursing research focusing on the ABMT experience for breast cancer patients is needed. External reliability of the research findings is compromised when such a select sample as seen in this study is used. We are unable at present to

state precisely why this under representation of minorities and medically under served populations exists nationwide in patients recruited for ABMT. One potential reason may be economic barriers related to the cost of ABMT. ABMT may cost between $80,000 to over $150,000, as compared with the cost of conventional chemotherapy which is between approximately $15,000 to $40,000. (United States General Accounting Office, 1996). Other potential reasons for this under representation are issues related to access to ABMT, education regarding the ABMT process, and lack of insurance coverage. Clearly we need to assess why these populations are under represented in this treatment modality and to develop and test appropriate intervention strategies to increase accrual.

Conclusions

Breast cancer patients scheduled for ABMT experience low grade pain intensity, psychological distress, and alterations in health status and coping during the pre-admission period. Health care providers need to be aware of these potential breast cancer patient experiences in order to promote appropriate assessments, provide effective care, and make necessary referrals. Further research needs to be directed toward appropriate interventions to assist ABMT patients to cope with the many challenges related to pain, psychological distress, and alterations in coping and health status which they experience during the pre-ABMT phase.

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Table 1. Demographic Characteristics of the Sample (n = 83)

Demographic Characteristics	n	%
Sex		
Female	83	100
Ethnicity		
Caucasian	72	88
African-American	6	7
Other Minorities	4	5
Marital Status		
Married	61	75
Single	11	13
Divorced	10	12
Education Completed		
High School	16	19
Some College	23	28
College Graduate	26	32
Graduate Degree	17	21
Religion		
Catholic	19	24
Protestant	41	51
Jewish	6	7
Other	11	14
None	3	4
Patient Lives With		
Spouse	59	73
Other	9	11
Self	13	16
Average Yearly Income		
< $50,000.	24	32
≥ $50,000.	50	68
Occupation		
Professional	45	62
Non-Professional	28	38
Work Status		
Employed	58	73
Unemployed	22	27
Age		
Mean	44.47	
SD	± 7.29	
Range	22-59	

Note. Some patients chose not to answer all questions. Missing data excluded for percentage computation where applicable.

Table 2. Mean Pain Intensity Ratings During the Pre-ABMT Period (n = 83) (54% of the Subjects Experienced No Pain)

Pain Intensity	Mean ± SD	Median	Range
Affective	3.45 ± 4.14	2.5	1 - 24
Sensory	4.47 ± 3.67	4.0	1 - 20
Total Score	6.92 ± 6.86	6.0	1 - 44

Table 3. Sensory and Affective Words Chosen to Describe the Quality of Pain During Pre-ABMT Period (n = 83)

Sensory Words	n	%	Affective Words	n	%
Aching	21	25	Annoying	22	26
Sore	20	24	Tiring	14	17
Dull	11	13	Troublesome	8	10
Hurting	6	7	Nagging	8	10
Burning	5	6	Agonizing	3	4
Shooting	4	5	Terrifying	2	2
Tearing	3	4	Miserable	2	2
Stabbing	2	2	Torturing	1	1
Radiating	2	2	Unbearable	1	1
Sharp	2	2	Killing	1	1
Cramping	2	2			
Crushing	1	1			
Pressing	1	1			

Table 4. Locations of Pain Complaints During Pre-ABMT Period (n = 83)

Pain Locations	n	%
Vagina	16	19
Chest	12	14
Shoulder	11	13
Arm	8	10
Neck	5	6
Abdomen	4	5
Generalized	4	5
Breast	3	4
Joint/Hand	3	4
Other	3	4
Mouth	2	2
Head (ache)	2	2
Rectum	1	1

Table 5. Mean Coping Strategies Questionnaire (CSQ) Ratings During Pre-ABMT Period (n = 83)

Items on CSQ	Mean ± SD	Range
Ignoring Pain	14.26 ± 7.37	1 - 34
Coping Statements	22.15 ± 6.19	7 - 36
Reinterpreting Pain	6.79 ± 6.81	0 - 27
Diverting Attention	17.08 ± 7.66	1 - 34
Praying and Hoping	19.31 ± 8.23	2 - 35
Catastrophizing	6.22 ± 5.87	0 - 26
Behavioral Activity	17.36 ± 5.73	3 - 31
Ability to Control Pain	3.99 ± 1.11	1 - 6
Ability to Decrease Pain	3.80 ± 1.29	1 - 6

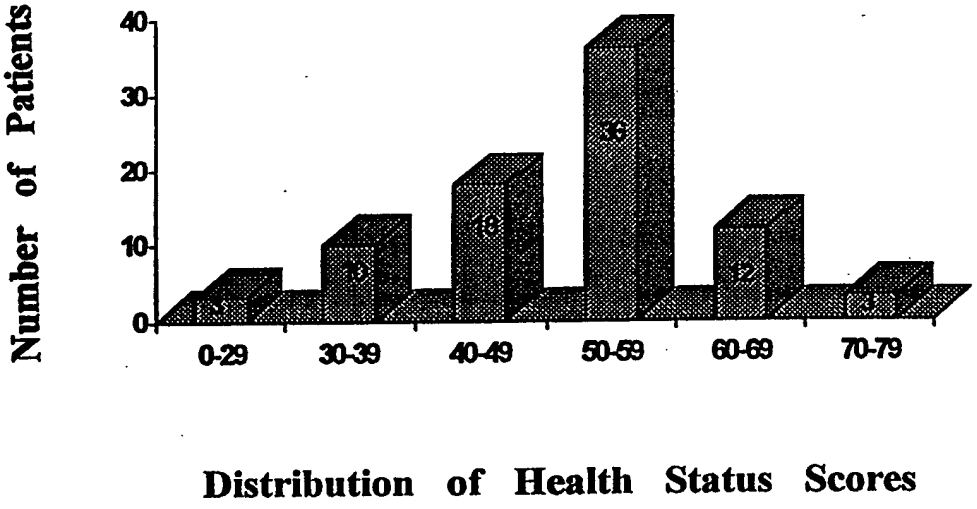

Figure 1. Distribution of Health Status Scores

Table 6. Correlation Between Pain and Selected Variables (n = 83)

	Pain (Overall Intensity)	Pain (Affective)	Pain (Sensory)	Anxiety (State)	Depression	Catastrophizing	Coping	Health Status (Total)	Physical Functioning	Role Functioning	Social Functioning	Mental Health	Health Perception	Pain
Pain (Overall (Intensity)	1													
Pain (Affective)	.71***	1												
Pain (Sensory)	.67***	-.04	1											
Anxiety (State)	-.07	-.13	.03	1										
Depression	.02	-.12	.17	.61***	1									
Catastrophizing	.08	-.09	.22	.29**	.29**	1								
Coping	.16	.22*	-.006	-.22*	-.19	-.20	1							
Health Status (Total)	-.20	.004	-.33**	-.56**	-.73***	-.43***	.12	1						
Physical Functioning	-.16	-.0005	-.24*	-.12	-.22*	-.23*	.10	.44***	1					
Role Functioning	.03	.21*	-.19	-.18	-.33**	-.21	.23	.50***	.65***	1				
Social Functioning	-.15	.11	-.33**	-.33**	-.57***	-.30**	.17	.73***	.42***	.47***	1			
Mental Health	-.05	.08	-.16	-.66***	-.71***	-.27*	.13	.76***	.04	.17	.44***	1		
Health Perception	-.23*	-.06	-.27*	-.41***	-.54***	-.39***	.04	.85***	.23*	.30**	.49***	.49***	1	
Pain	-.16	.04	-.28**	-.09	-.32**	-.39***	.02	.57***	.40***	.37***	.59***	.20	.41***	1

*p < .05 **p < .01 ***p < .001

Appendix D

The Effectiveness of the Comprehensive Coping Strategy Program on Clinical Outcomes in Breast Cancer Autotransplantation Patients

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Autotransplantation (AT) for breast cancer exploits the steep dose-response relationship through use of high-dose chemotherapy followed by rescue with either bone marrow or peripheral blood stem cell transplantation to prolong survival and disease-free survival (1). Breast cancer patients who undergo this treatment must cope not only with a life-threatening medical procedure, but also with multiple, interrelated symptoms including pain, fatigue, psychological distress, and nausea (2,3). Compounding these stressors is the fact that patients often attempt to cope with the treatment and symptom experience in a geographically distant, unfamiliar medical center. Health care professionals must understand the symptom experience of the breast cancer AT patient to provide appropriate care planning, implementation, and evaluation.

The purpose of this study was to examine the effectiveness of the Comprehensive Coping Strategy Program (CCSP) on pain, fatigue, psychological distress, and nausea in female breast cancer patients who undergo AT. The hypothesis addressed in this study is there is a significant difference in the pain, fatigue, psychological distress, and nausea between patients with breast cancer who receive AT and the CCSP and patients with breast cancer who receive AT but do not receive the CCSP.

Literature Review

Pain

Pain is a significant problem for a large number of breast cancer patients (4,5). This pain may be acute, as experienced prediagnosis, and after lumpectomy or

mastectomy surgery, axillary node dissection, and chemotherapy, or may be chronic and long-term in nature (6,7). Treatment-related breast pain from surgery and chemotherapy is related to breakdown of the skin integrity. Gaston-Johansson reported that patients who received high-dose chemotherapy and AT experienced mild to moderate pain (3). Miaskowski and Dibble (4) found that 47% of breast cancer patients receiving chemotherapy treatment in the outpatient setting reported cancer-related pain. Patients rated their pain as moderate to severe on a daily basis that affected their activities of daily living and quality of life (QOL).The majority of patients in this group were found to have treatment-related pain from post-surgical neuropathic pain syndrome (56%) and cancer-related pain from bone metastasis (26%).

Pain is more complex than only physical symptoms of breast cancer and has psychological implications as well. Breast cancer patients who experience cancer-related pain have significantly more depression, anger, fatigue, and symptom distress, and lower interpersonal well-being than pain-free patients (4,8). Cancer survivors have noted that fatigue was a precursor to decreasing their tolerance to pain and that pain was a physical symptom related to increasing fatigue (9). Pain is often used as a metaphor for advancing disease and death for both patients and family members (9,10).

Many patients have reported using nonpharmacologic approaches in an attempt to reduce discomfort, including relaxation, imagery, massage, exercise and physical therapy. A pilot study performed by Arathuzik (11) found that teaching both

inpatient and outpatient breast cancer patients relaxation, visualization, and cognitive coping skills in busy clinical settings was effective in relieving some pain. These cognitive and physical approaches have proven effective in relieving pain in both breast and lung cancer patients, but need evaluation in clinical trials (10,11,12,13).

Regardless of the type of pain relief intervention used, it is important to remember that patients need to cope with the extreme psychological distress arising from their cancer experience to allow for actual pain relief to occur. Pain frequency has been found to correlate significantly with fatigue, vigor, and depression (14). The interrelatedness of pain and other symptoms experienced by breast cancer AT patients makes symptom management a challenge for clinicians.

Fatigue

Fatigue is the most commonly reported symptom associated with cancer and it is the most commonly reported side-effect of chemotherapy (15,16). Fatigue is often an "...initial and ongoing symptom of cancer which is exacerbated during periods of active treatment as well as in advancing neoplasia" (17, p. 177). Numerous treatment and disease-related factors contribute to fatigue including surgery, chemotherapy, radiation therapy, interferons, immunosuppression, infections, anorexia, weight loss, psychological distress, chronic pain, and alterations in sleep patterns (18,19).

Fatigue is a major, debilitating symptom which can have a dramatic effect on the lives of breast cancer patients (20). This symptom is a serious iatrogenic side effect associated with chemotherapy with cell destruction end products, nausea, and

vomiting thought to be contributing factors (17). Nursing literature reviewed from 1978 through 1993 focusing on chronic fatigue in cancer patients receiving chemotherapy contained 18 reports of fatigue prevalence, intensity, and correlates (21). Prevalence estimates derived from several of these fatigue studies ranged from 80% to 99% (21).

Chemotherapy-related fatigue is cyclical, usually beginning 1 to 2 weeks post-chemotherapy administration in conjunction with the hematological nadir, and then decreasing only to begin with the following subsequent chemotherapy cycle (22,23). This cyclical nature of fatigue has a severe impact on a patient's mood and ability to perform daily activities (21). Irvine, Vincent, Graydon, Bubela, and Thompson (15) found that as fatigue increased so did symptom distress, mood disturbance, and loss of ability to perform usual physical, recreational, vocational, home, and social activities. Such changes in lifestyle may cause the patient to experience unnecessary anxiety and depression in addition to the already life-threatening illness. A further finding was that fatigue was not significantly correlated with duration of disease status or with stage of disease. Fatigue may also lead to decreased patient QOL (24).

Chemotherapy which crosses the blood-brain barrier has neurotoxic properties which may affect neurotransmission and thus produce fatigue (25). Fatigue has been linked with impairment of cognitive functioning and impaired perception and thinking ability (26). Lee (27), in a study of women's responses to environmental demands, found that depression or anxiety were more significantly related to both fatigue and vitality than were external stresses.

Researchers have reported common strategies used by patients to combat their chemotherapy-induced fatigue, such as rest and decreasing the number of activities. Graydon (28) found that patients undergoing chemotherapy who were able to use effective fatigue relieving strategies experienced less fatigue compared to those patients who employed less effective fatigue relieving strategies, such as eating, drinking, or watching television.

Fatigue and its affects on mood, concentration, and activities of daily living has primarily been investigated relating to chemotherapy and radiation therapy. Few studies have examined the fatigue experience longitudinally from one treatment modality up through and in preparation for another treatment modality. There is also a paucity of research regarding the subjective nature of fatigue. As patients with breast cancer live longer, fatigue may be expected to become an increasing problem. The understanding and management of fatigue is clearly one of the greatest challenges to oncology nurse researchers and clinicians today (29).

Anxiety and Depression

Anxiety and depression are common responses to the diagnosis of and treatment for breast cancer (30,31,32). Up to 71% of the women treated with chemotherapy for breast cancer reported psychological distress, including anxiety, preparing for the future, sadness, and depression at the end of treatment. Chemotherapy represents a prolonged threat to a patient's mortality and functioning causing additional psychological distress after breast surgery. A Swiss study performed by Maraste (33) indicated that 14% of patients who underwent adjuvant

chemotherapy following breast-conserving surgeries and mastectomies experienced morbid anxiety scores. Coscarelli-Shag et al. (34) identified the following major sources of psychological distress for breast cancer patients at one month post-diagnosis: a) anxiousness while waiting for test results and having to undergo additional diagnostic tests; b) worries over whether the cancer was progressing; c) concern about ability to take care of self; and d) concern about how the family would manage if the patient died. Massie (35) found from an analysis of 20 years of research regarding depression in cancer patients that approximately 25% were depressed and up to 50% exhibited some symptoms of depression. Elevated levels of depression and anxiety may persist in a minority of breast cancer patients even years after the diagnosis (36).

Spiegel, Sands, and Koopman (14) explored the relationship between pain and depression in 96 subjects - 48 in the high pain group and 48 in the low pain group. Prevalence of depression was found to be significantly higher in the high pain rather than in the low pain group (14). Pain intensity was also found to correlate significantly with fatigue, vigor, and total mood disturbance. Aass, Fossa, Dahl, and Moe (37) investigated the prevalence of anxiety and depression in 716 cancer patients using the Hospital Anxiety and Depression Scale, the EORTC-QLQ-C33, and an ad hoc depression questionnaire. The prevalence of depression was 9% as assessed by the HADS with age or gender having no influence on the occurrence of depression (37). The prevalence of depression increased with distant metastases, with the time period of less than one month from diagnosis, and was seen with a relapse or disease

progression (37).

The importance of adhering to a strict schedule of chemotherapy treatment to halt spread of cancer has been well documented, and therefore addressing patients' anxiety and depression over the course of treatment is of paramount importance. Several research groups have confirmed that patients with a moderate degree of psychological distress may be more motivated to participate in chemotherapy treatment (33,38). Patients were found to have diminished anxiety towards the end of chemotherapy, but continued to have specific anxieties regarding the termination of the close medical supervision from their health care team, and the possibility of cancer recurrence (33,38)

Nausea

Nausea is a common symptom associated with chemotherapy treatment (39). The literature shows several main responses associated with the impact of nausea in cancer patients including anxiety, depression, autonomic nervous system responses, social withdrawal, and food aversion (40,41).The experience of nausea is usually accompanied by increased salivation, swallowing, and tachycardia (42). The numerous physical side-effects of chemotherapy have an immediate and negative impact on a patient's QOL. Many studies have found that nausea is significant independent indicator of QOL on the first day and a few days following administration of chemotherapy (43).

Pharmacological and non-pharmacological interventions have been used to attempt to manage nausea. Non-pharmacological interventions which have been used

to reduce nausea are distraction, progressive muscle relaxation, guided imagery, biofeedback, and hypnosis (38,44). The most effective treatment strategies for managing nausea combine these approaches since neither is totally effective when used alone (42). Limitations of previous research studies include sample sizes and inclusion of few minorities.

Theoretical Support for a Comprehensive Coping Strategy Program

Nonpharmacologic therapies are most frequently used to help control a wide range of symptoms such as pain, fatigue, anxiety, depression, and nausea (38,42). Earlier research and preliminary studies of Dr. Gaston-Johansson support the use of the CCSP (45,46,47). The use of combined treatment has been viewed positively. However, as Woods (48) noted, often a nursing intervention demonstrates no positive effects because the treatment is not effective enough. To create a powerful treatment, it is logical to test a combined intervention such as the one proposed in this study. Because pain and fatigue are multidimensional experiences, logic suggests using a multimodal strategy to effect a change in these symptoms (49). This is the first time that the unique combination of preparatory information, cognitive restructuring, and relaxation with imagery has been evaluated in breast cancer patients undergoing AT to improve clinical outcomes.

The purposes of the CCSP are the following: a) give the patient objective and subjective information about what may be expected regarding side effects of high-dose chemotherapy and AT treatment in order to increase control and decrease symptoms and discomfort; b) enhance the coping ability of the patient by teaching

them to recognize and avoid distorted thinking and catastrophizing, and how to use positive coping self-statements; and c) teach the patient how to use relaxation with imagery. Each of the components of the CCSP has been found to be effective in reducing multiple symptoms. Each of the four components of the CCSP has been tested separately and found to be effective in reducing individual symptom associated with diagnosis and treatment, but no study was found that combined these particular strategies to treat breast cancer patients undergoing AT. Therefore this is the first study to examine the effectiveness of the CCSP in this population.

Symptoms associated with high-dose chemotherapy can be distressing, and therefore it is important to teach the patient the CCSP prior to treatment, and to regularly reinforce the CCSP during the course of treatment (50). Giving patients information about what to expect in relationship to a specific procedure and treatment side effects is an important factor in achieving positive clinical outcomes (50,51). A well developed body of knowledge, earlier referred to as preparatory sensory information, is now termed concrete objective information (COI). The use of COI includes providing the patient with concrete and objective information that describes the expected subjective and objective experiences. The theory underlying the use of COI is that helping a person to focus his attention on objective features of a situation allows him to more easily process information, to understanding the situation, and to

cope (50,51). Post mastectomy breast cancer patients undergoing AT are appropriate candidates for preparatory information because the treatment side effects are both short and long term, and the COI might be expected to increase their use of positive problem-solving activities, increase their ability to deal with the event, and select more appropriate coping strategies. It has been demonstrated that combining concrete information and subjective information is more effective than using them separately (48,49).

Coping is defined as constantly changing cognitive and behavioral efforts used to manage specific external and /or internal demands that are appraised as taxing or exceeding the resources of a person (52). Positive coping strategies refer to internal thoughts and behaviors people use to manage undesirable symptoms, their pain, or their emotional reactions to the pain and to reduce emotional distress (52). Catastrophizing, a negative coping strategy, is defined as a method of cognitive coping characterized by negative self-statements and thoughts about the future (52) Negative thoughts have been associated with negative health outcomes. This theory is used as a basis for developing the coping aspects of the CCSP program and is complimentary with the use of preparatory information.

Progressive muscle relaxation and imagery (53) have been found to help patients to either escape the problem or think of the problem in alternative ways.

Several studies have shown that relaxation and imagery appear to reduce the sensory experience of pain, and have equivocal effects on affective measures. Cognitive behavioral training helps develop coping skills and lessens the anxiety and depression which may exacerbate the symptom (49). The use of other psychological interventions such as relaxation techniques incorporated into a comprehensive coping strategy program (CCSP) may allow for further emotional relief in alleviating a patient's fatigue. The efficacy of relaxation and psychological counseling is well established (49).The mechanisms of action regarding behavioral therapies and the attenuation of pain required further elucidation (49). Previous studies that have tested the effects of relaxation and imagery on cancer pain have been limited by weak theoretical frameworks, small sample sizes, and lack of control over the intervention.

Methodology

Design

This study used an experimental design with random assignment to one of two possible groups. Thus it was a randomized, controlled prospective clinical trial. Participants were randomized to one of the following two groups after written informed consent had been obtained: Group I: Patients scheduled for AT who received a CCSP (treatment group); or Group II: Patients scheduled for AT who did not receive the CCSP (control group). Both groups received usual medical treatment

and nursing care.

The study was approved by the Institutional Review Board prior to participant accrual. All participants were recruited by either the physician co-principal investigator or the oncology clinical nurse specialist (CNS) co-investigator during a regularly scheduled pre-AT Medical Oncology Outpatient Clinic visit. All participants had been accepted into the AT program prior to the invitation to participate in this study. The CCSP was taught to patients in the treatment group at least two weeks prior to admission to hospital, before treatment with high-dose chemotherapy and AT. The CCSP was reinforced on the same day the patient was admitted to hospital, 2 days after completion of chemotherapy, and 7 to 9 days after the AT.

The subjects completed the questionnaires at baseline in a quiet, comfortable room located in the outpatient clinic. The CNS remained with the patient during this time. The subjects completed the questionnaires on BMT day -2 and BMT day +7 in their hospital rooms It took approximately one hour for the subjects to complete the questionnaires.

Patients and Setting

A consecutive sample of 128 women with stage II, stage III, or stage IV breast cancer who were scheduled for AT at an urban designated comprehensive National Cancer Center located in Eastern United States agreed to participate in the

study. Once recruited, the following eligibility criteria were used for participation in the study: subjects in both groups had to undergo the AT and those in the treatment group had to participate in the CCSP. Eighteen subjects did not meet this criteria (3 had their AT canceled, 10 subjects refused to participate after they had signed consent forms, and 4 subjects were too ill to participate in the CCSP). The final sample was 111 subjects.

Instrumentation

Sociodemographic variables: The Sociodemographic Questionnaire used in this study included the following items: age; gender; race/ethnicity; marital status; educational level; religion; patient living arrangements; average yearly household income; occupation; work status; and household income; type of chemotherapy, breast cancer stage., and the subjects previous experience of using relaxation and coping strategies.

Pain: The Painometer © (POM), which was designed to assess patients' overall pain intensity and intensity of the sensory and affective components of pain, as well as the quality of pain (54). The POM is a hard, white plastic tool which measures 8 inches long, 2 inches wide, and 1 inch thick. It is light weighted and is held easily by the subject. A list of 15 sensory and 11 affective pain descriptors is located on the front side of the POM and a 100mm VAS with a moveable marker (POM-

VAS) is located on the back side of the POM. An intensity value (from a low of "1" to a high of "5") is predetermined for each sensory and affective word located on the POM-WDS. A maximum score of 36 can be obtained for the sensory component of pain and of 34 for the affective component. A total score can be obtained by adding the sensory and affective scores. High correlations were found between the initial and the repeat pain intensity ratings on the POM-VAS ($r = 0.88$, $p < 0.001$) and the POM-WDS ($r = 0.84$, $p < 0.001$) (test-retest reliability). Correlations between the POM-WDS and the McGill Pain Questionnaire ($r = 0.69$, $p < 0.001$) and POM-VAS ($r = 0.85$, $p < 0.001$) supported the concurrent validity of the POM-WDS. Construct validity was also supported for the POM by showing that pain scores decreased significantly from POM-WDS ($t = 5.53$, $p < 0.001$), and POM-VAS ($t = 6.18$, $p < 0.001$) after the treatment with pain medication. The POM took about 2 minutes to complete.

Nausea : The severity of nausea was measured using a visual analogue scale (VAS). The VAS is a line, usually 100mm in length, with anchors at each end that indicate no nausea and nausea as severe as can be. When used properly, the VAS is a reliable, valid, and sensitive self-report tool for studying subjective symptoms (55).

Fatigue: Fatigue was measured using the Fatigue Visual Analogue Scale (VAS). The Fatigue VAS is a 100mm vertical visual analogue scale anchored with

"completely exhausted" and "no fatigue". The subject marks with a horizontal mark through the vertical line indicating the degree of fatigue which she is currently experiencing. Reliability and validity of the Fatigue VAS have been demonstrated.

Psychological Distress: **a) Anxiety:** The State-Trait Anxiety Inventory (STAI) (102) will be used as one measure of psychological distress. The STAI consists of two separate self-report scales for measuring state and trait anxiety (56). State anxiety is a transitory emotional response to a stressful situation. Trait anxiety reflects a stable predisposition to anxiety as determined by a personality pattern. Each scale consists of 20 statements related to emotions and requires 5 to 10 minutes to complete. Respondents rate themselves in relationship to the statement on a Likert scale from 1 to 4. The total score is the sum of all 20 responses and ranges from a minimum score of 20-39 (low anxiety), 40-59 (moderate anxiety), to a maximum score of 60-80 (high anxiety). Scores are reported to be considerably higher under stress conditions than under normal conditions (56). Test-retest reliability correlations reported for the trait scale ranged from .73 to .86, as opposed to the range of .16 to .54 for the state scale (56). Construct validity of the SATI has been demonstrated (56); **b) Depression:** Beck's Depression Inventory (BDI) (103) will also be used to measure psychological distress. The BDI consists of 21 items that describe particular symptoms of depression (57) Subjects respond to a Likert-type scale by rating each

item 0 (no symptom) to 3 (severe or persistent presence of the symptom). Scores ranging from 0 to 9 are normal, 10 to 15 mild depression, 16 to 23 moderate depression, and 24 to 63 severe depression. The total score (range 0 to 63) is obtained by summing the 21 responses. Test-retest correlations of the BDI ranged from .60 to .90 in non-psychiatric patients (57). Content and construct validity have Been demonstrated for the BDI.

Statistical Analysis

Preliminary analysis of the data included exploratory data analysis to ascertain data quality, handle outliners and missing data, and measure group differences among sociodemographic characteristics, disease stage, and types of chemotherapy. Descriptive statistics (frequency, percent, mean, median, and standard deviation) were used to describe the sample and responses to the instruments. Final phase of analysis included multiple regression analysis to assess differences between CCSP and control groups after adjusting for covariates and controlling for demographic variables.

Results

Sample Characteristics

Fifty two (47 %) patients received a CCSP and 58 were in the control group (Table 1). The majority of the patients were 41 to 50 years old. Ninety percent in the CCSP group compared to 57% in the control group were married ($P < 0.001$). The

CCSP group had a statistically significant lower annual household income ($P < 0.05$) than the control group. Forty percent in the CCSP group compared to 21% in the control group had practiced some earlier coping methods ($P < 0.05$). There were no statistically significant differences between the groups with regard to stage of the disease and type of chemotherapy treatment. The rate of patient accrual at follow-up since AT was not found to differ significantly between the two groups of subjects. There was a statistically significant difference in death rate between the patients receiving the CCSP and the control groups ($p < 0.05$).

Pain

All mean pain intensity scores were low. The sensory pain scores were slightly higher than the affective scores on BMT day +7 (Table 2). Total pain scores were lowest on BMT day -2 for the treatment group, and reached their peak on BMT day +7. Pain scores reported gradually increased and reached their peak intensity level on BMT day +7 for both the treatment and control groups. There were no significant differences between the groups with regard to the intensity of the different pain scores.

The most frequent words chosen by the subjects to describe the sensory component of pain were aching (25%); sore (24%); and dull (13%). The most frequent affective words were annoying (26%), tiring (17%), troublesome (10%),

and nagging (10%). Pain was most frequently located in the vagina (19%), chest (14%), shoulder (13%), and arm (10%).

Nausea

In the CCSP group, nausea was more severe on BMT day -2 than on BMT day +7. The opposite was the case in the control group with nausea reaching it's greatest intensity level on BMT day +7. On BMT day +7 nausea was 23 points higher in the control group compared to the CCSP group. There was a statistically significant difference between the groups regarding nausea on day +7 with the CCSP treatment group reporting less nausea than the control group $F(1, 72) = 5.50$, $p<0.05$). After controlling for demographic variables and the nausea score on BMT day -2, there was still a group difference on BMT day +7 with the CCSP group showing statistically significant lower scores than the control group ($B=-16.94$, $\beta = -.28$, $p<0.05$).

Fatigue

Fatigue reached it's peak on BMT day -2 for both groups with fatigue increasing by 10.80 points in the CCSP group from baseline to BMT day -2 compared to 20.33 points in the control group. On BMT day +7, the control group rated their fatigue as 9.44 points higher than the CCSP group. There were no statistically significant differences in fatigue levels between the groups on BMT day -2 . On BMT

day +7, after controlling for fatigue on BMT day -2, there was a significant difference between the groups F (1, 63,) = 4.01, $p<0.05$. However, after controlling for demographic and fatigue on day -2, there were no statistically significant differences between the groups. When an index of nausea + fatigue was created for BMT day +7, and after controlling for demographic variables, there was a significant difference between the groups with the control group having higher scores (B= -26.23, Beta-.27, $p<0.05$).

Psychological Distress

Anxiety remained constant for the control group from baseline to BMT day +7 but decreased by 9 points in the CCSP group from baseline to BMT day +7. Depression increased in both groups over time and reached its's peak level in the control group on BMT day -2. There were no statistically significant differences between the groups with regard to psychological distress.

Discussion

The sample consisted of a select group of highly educated, married Caucasian women. This sample corresponds to the national demographic trend for women who chose to undergo AT. It is interesting to note that 40% of the treatment group had used coping methods prior to taking part in this study.

Although low grade pain was reported by the subjects, it is important to remember

that any severity of pain may cause great symptom distress to the patient. The location of pain reported in the chest and shoulder may be related to manipulation of the nerves and muscles in the chest during mastectomy. Pain located in the vagina has been found in an earlier study by Gaston-Johansson et al. (F. Gaston-Johansson, personal communication, 1998) and may be related to atrophic vaginitis. This vaginal inflammation may be ammenable to pain management and should be further explored.

The CCSP was found to be effective in reducing nausea and fatigue on BMT day +7. This is an important finding because BMT day +5 was found to be the time period of greatest suffering for AT patients (3). The ability of the CCSP to decrease multiple symptoms may lessen this suffering for the patients during this early post-AT time period.

The statistically significant difference in death rate between the treatment and the control group is an important finding. Further statistical analysis is planned to examine this result including exploration of selected sociodemographic factors.

Conclusions

The CCSP's greatest effectiveness may correspond to the time period of the breast cancer AT patient's greatest morbidity. This finding derives logically from the theoretical framework and argues for the CCSP being a powerful intervention which is appropriate for use in the AT breast cancer population.

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Table 1. Demographic Characteristics of the Sample (n = 111)

Attributes		CCSP (N=52) n(%)	Control(N=58) n(%)
Age	22-40 years	11(21.2)	17(29.8)
	41-50 years	26(50.0)	32(56.2)
	51 years and over	15(28.8)	8(14.0)
Race -	White	46(88.5)	48(82.8)
Employment Status -	Employed	38(73.1)	36(62.1)
Marital Status -	Married	47(90.4)	33(56.9)***
Education	=< High School	8(15.4)	10(17.5)
	Some College	10(19.2)	18(31.6)
	College/Grad.degree	34(65.4)	29(50.9)
Occupation –	Professionals	34(65.4)	32(55.2)
Income –	Less than 50K	10(19.2)	22(37.9)*
Cancer Stage	Stage II	8(15.4)	13(22.4)
	Stage III	32(61.5)	17(29.3)
	Stage IV	12(23.4)	28(48.3)
Chemotherapy type	I	22(42.3)	30(56.9)
	II	30(57.7)	25(43.1)
Prior Coping Methods		21(40.4)	12(20.7)*
Prior Relaxation Methods		20(38.5)	18(31.0)

@ Comprehensive Coping Strategy Program
* P <0.05 *** P<0.001

Table 2. Symptoms Experienced at Baseline, 2 Days Before ABMT (Day -2) and 7 Days after ABMT (Day +7) (n = 111)

		Baseline		Day -2		Day +7	
Symptom	Group	Mean	SD	Mean	SD	Mean	SD
Pain							
Affective	Tx	1.38	3.72	1.66	3.49	2.70	3.75
	C	2.05	4.41	2.67	5.58	2.45	4.54
Sensory	Tx	2.12	4.48	1.10	2.03	4.46	5.50
	C	2.63	3.41	2.18	3.81	3.36	5.18
Total	Tx	3.50	7.66	2.76	4.69	7.16	8.45
	C	4.68	7.11	4.84	8.22	5.82	9.32
VAS	Tx	5.89	13.08	14.50	15.36	29.50	28.23
	C	6.07	11.42	11.62	7.89	19.86	24.17
Fatigue	Tx	31.35	26.00	42.15	26.63	40.92	27.36
	C	31.35	28.23	51.68	28.64	50.36	27.25
Nausea	Tx	3.94	10.63	27.60	27.92	19.65	25.16
	C	5.80	16.86	25.74	28.09	32.20	32.51
Anxiety	Tx	40.16	12.15	39.50	10.41	30.65	11.53
	C	40.93	12.42	41.14	11.59	40.26	11.00
Depression	Tx	9.17	6.05	10.05	6.31	10.33	6.86
	C	11.44	7.88	13.56	11.50	12.25	8.01

Appendix E

The Effects of a Comprehensive Coping Strategy Program on Mortality

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INTRODUCTION

Breast cancer in the United States is estimated to be diagnosed in 187,700 women in 1998; 43,500 women are predicted to die from this disease [1]. Survival rates in breast cancer are correlated with the extent of disease [2], as evidenced by the ten year survival rate of 65% to 80% for women with disease confined to the breast decreasing to a median survival rate of approximately 2 years and a 2% to 5% probability of 5-year survival for women with metastatic disease [2]. The estimated number of deaths from breast cancer in the U.S. for 1998 is 16 % of all types of cancer in women. Mastectomy followed by high dose chemotherapy and autotransplant is one treatment modality developed in response to the challenge of improving mortality and extending survival.

Autotransplantation which exploits the steep dose response tumoricidal effect of high dose chemotherapy in breast cancer followed by rescue with the reinfusion of either the patient's own cryopreserved bone marrow cells (BMT) or peripheral blood stem cells (PBSCT). More than 5,000 autotransplants (AT) are performed annually wordwide[3]. The use of AT for breast cancer comprised 15% of transplants in 1989, increasing to 35% in 1994[4]. In 10%-30% of breast cancer patients with chemotherapy-sensitive, stage IV disease, results have shown disease-free survival at two to five years, following ABMT[5-7].

Although patients recognize that the AT may save their lives, many patients may suffer to the extent that they regret having the treatment[8-9]. Autotransplantation has been associated with multiple symptoms such as pain, fatigue, nausea, psychological distress and alterations in coping [10-17]. Anticipatory anxiety may be generated by knowledge that AT can lead to great physical and psychological distress including, but not limited to, the following: gastrointestinal complications - painful effects on the epithelial membranes of the oral cavity (mucositis, ulcerations), gastritis, diarrhea, nausea and vomiting; genitourinary complication - painful effects

on the mucosal epithelial membranes of the bladder wall (chemical cystitis); veno-occlusive disease; infection; high fever and sepsis; hemorrhage; renal complications; neurological complications; cardiac toxicities; alopecia with resultant effects on body image and fatigue, psychological distress and death[18] . These multiple symptoms, accompanied by psychological distress, and fear of death can all be seen as physiologic and psychologic stressors that greatly affect the patient's perceived health status, quality of life and coping abilities. Few studies have addressed the need for a comprehensive coping strategy program to help patients deal with the multiple symptoms and stressors associate with the diagnosis of cancer, side effects of chemotherapy and AT.

The purpose of this study was to determine if a comprehensive Coping Strategy Treatment Program had an effect on mortality in breast cancer patients treated with AT. The Comprehensive Coping Strategy Program (CCSP) is composed of preparatory information, cognitive restructuring and relaxation with imagery.

HYPOTHESIS

Patients with breast cancer who are treated with autotransplant and receive a Comprehensive Coping Strategy Program (CCSP) are less likely to die than patients with breast cancer who are treated with autotransplant and do not receive the CCSP.

DESIGN and METHODS

Design

This study used an experimental design with random assignment to one of two possible groups, thus it was a randomized, controlled prospective clinical trial. Participants were randomized to the following two groups after informed consent had been obtained. Both groups received usual medical treatment and nursing care.

Group I: Patients scheduled for AT who received a CCSP (treatment group)

Group II: Patients scheduled for AT who did not receive the CCSP (control group).

The CCSP was taught to patients in the treatment group at least two weeks prior to admission to hospital, before treatment with high-dose chemotherapy and AT. The CCSP was reinforced on the same day the patient was admitted to hospital, 2 days after completion of chemotherapy, and 7-9 days after the AT.

Patients and Setting

A consecutive sample of 127 women with stage II, stage III, or stage IV breast cancer who were scheduled for AT at an urban designated comprehensive National Cancer Center located in Eastern United States, agreed to participate in the study. Once recruited, the following eligibility criteria were used for participation in the study: Subjects in both groups had to undergo the AT and those in the treatment group had to participate in the CCSP. Eighteen subjects did not meet this criteria (3 had their AT canceled, 10 subjects refused to participate after they had signed consent forms, 4 subjects were too ill to participate in the CCSP). The final sample was 110 subjects.

Theoretical considerations Description of CCSP

Coping is defined as constantly changing cognitive and behavioral efforts used to manage specific external and /or internal demands that are appraised as taxing or exceeding the resources of a person [19]. Positive coping strategies refer to internal thoughts and behaviors people use to manage undesirable symptoms, their pain, or their emotional reactions to the pain and to reduce emotional distress[19]. Catastrophizing, a negative coping strategy, is defined as a method of cognitive coping characterized by negative self-statements and thoughts about the future[19] . Negative thoughts have been associated with negative health outcomes. The purposes of the CCSP are to (a) give the patient objective and subjective information about what may be expected regarding side effects of chemotherapy and AT treatment in order to increase control and decrease symptoms and discomfort; (b) enhance the coping ability of the patient by teaching them to recognize and avoid distorted thinking and catastrophizing; and how to use positive coping self-statements, and (c) teach the patient how to use relaxation with imagery. Each of the components of the CCSP have been found to be

effective in reducing multiple symptoms. Each of the 4 components of the CCSP have been tested separately and found to be effective in reducing individual symptom associated with diagnosis and treatment, but no study could be found that combined these particular strategies to treat breast cancer patients undergoing autotransplant. This however is the first study to combined these particular strategies to treat breast cancer patients undergoing autotransplant.

Instrumentation

The Sociodemographic Questionnaire used in this study included the following items: age; gender; race/ethnicity; marital status; educational level; religion; patient living arrangements; average yearly household income; occupation; work status; and household income; type of chemotherapy, breast cancer stage., and the subjects previous experience of using relaxation and coping strategies.

Statistical Analysis

Preliminary analysis of the data included exploratory data analysis to ascertain data quality, handle outliners and missing data and measure group differences among Sociodemographic characteristics, disease stage, types of chemotherapy, follow-up time since AT, and mean survival time. Chi-square statistics were used to measure the independent association of proportion between CCSP and their controls. In our second stage of analysis we assessed the likelihood of mortality (crude O.R. and 95% CI) between CCSP and their control, and the odds of death among categories that were considered as covariates in the subsequent multiple regression analysis. In this stage of analysis , we also combined the categories of follow-up period since AT, thus comparing the odds of death between 1 - 3 years of follow-up and those who were followed up to one year since receiving AT. In addition to the bivariate analysis, we assessed group differentials in survival time since AT using Kaplan-Myer survival curves (Fig. 2). Our final phase of analysis included multiple logistic regression analysis where the probability of mortality was assessed between CCSP and control groups after adjusting for all the covariates in the preliminary analysis. All analytical phases were carried out using

SPSS®[20].

RESULTS

Fifty two (47 %) patients received a CCSP and 58 were in the control group (Table 1). The majority of the patients were 41 to 50 years old. There was a statistically significant difference in death rate between the patients receiving the CCSP and the control groups ($p < 0.05$). Ninety percent in the CCSP group compared to 57% in the control group were married ($P<0.001$). The CCSP group had a statistically significant lower annual household income ($P<0.05$) than the control group. Forty percent in the CCSP group compared to 21% in the control group had practiced some earlier coping methods ($P< 0.05$). There were no statistically significant differences between the groups with regard to stage of the disease and type of chemotherapy treatment (Fig. 1). The rate of patient accrual at follow-up since AT was not found to differ significantly between the two groups of subjects.

A total of 16 patients (14.5%) had died when follow up was carried out. When stratified by group, 4 patients in the CCSP group (7.7%), compared to 12 in the control group[(20.7%) had died at follow up. The mean survival period was 341 days for the CCSP group compared to 233 days for the control group at follow-up. The odds ratio for mortality among the CCSP group was 0.32 ($P<0.05$) (table I).

Mortality

Table II describes the distribution of metastatic stages, types of chemotherapy received, follow up period since receiving AT and potential socio-demographic risk factors and their association with mortality. It also displays the crude odds ratio and its 95% confidence interval for mortality between CCSP patients and controls. CCSP patients were 11 times less likely to die than their controls. Patients who were followed up two to three years since AT were 8.5 times more likely to die than those who had their AT up to one year at follow up. A combined follow up period of one to three years placed the patients at a mortality risk of 4.5 (95% CI: 1.0-21.1; $p = 0.05$). Additionally patients who had a metastatic stage IV breast cancer were 9 times

(95% CI: 1.0-77.5; $p < 0.05$) more likely to die than patients diagnosed with stage II disease. All of the above variables with significant association with mortality and traditional socio-demographic factors were subsequently entered into a multiple logistic regression model for measuring the final group differential in mortality. Table III shows that CCSP patients were 11% less likely to die (P=0.05) when adjustments were made for demographics, metastatic stage, type of chemotherapy and previous practice of coping and relaxation methods, and follow up period of 2 to 3 years.

Figure 2 presents the survival probabilities at follow-up since AT between CCSP and the control groups. In general, the CCSP group shows a better chance of survival than the control group. Furthermore, the control group had a larger decline in the survival slope between 200 to 400 days at follow up since AT than the CCSP group, thus widening the overall difference in survival between the groups at 3 year follow up.

DISCUSSION

As hypothesized, patients with breast cancer who underwent bone marrow transplant and received the CCSP, where less likely to die than the comparison group (7.7% vs 20.7%). This difference was both clinically and statistically significant. Trends in statistical significance between groups during the multivariate analytic phase were noted ($p = 0.05$). These results appear to indicate that the CCSP treatment may have been effective. It appears from our study, that the probability of survival did not diverge until about one year following AT. The demographic characteristics of the sample did not influence the findings related to mortality, non did the stage of the disease or the type of chemotherapy.

The results of survival between groups need to be interpreted with caution. All patients have not been in the study for the same length of time regardless of group assignment. The mean survival time which was 341 days for the CCSP group and 233 days for the control group (table I) could be a function of the patients'

length of time in the study. For this reason we introduced follow up since AT as a covariate. Entry of this variable into the final model reduced the mortality likelihood for the CCSP group from 15% to 11% and lowering the p value from 0.06 to 0.05. It is possible to obtain statistically significant differences between groups in mortality once the participants have been in the study for a longer period of time than the current follow up period.

The emphasis of the CCSP was to help patients cope with multiple symptoms and stress while improving their quality of life and survival. At no time did our research team intend for the CCSP to influence the course of the disease or the mortality of the patients. In light of our findings, we are however, faced with the difficult task of trying to explain our results and how the CCSP might have had an effect on survival and mortality.

Psycho-Physiologic perspective

Breast cancer patients who receive high dose chemotherapy after mastectomy experience a wide variety of symptoms such as: pain [21-23] fatigue [17], psychological distress, and nausea and vomiting [24-26]. These symptoms are interrelated and affect in excess of 70% of patients [22-23]. These symptoms can be quite severe and lead to a premature withdrawal from treatment [24-28], decreased health status and quality of life (QOL), and even death [24-27]. Despite effective state-of-the-art treatment of these symptoms, including behavioral therapy [23,24], there is evidence that patients still experience these distressing symptoms [23,24,28] The devastating effects of multiple symptoms may be linked to the course of cancer via the neuroendocrine and immune systems. Both animal and human studies have shown that pain [29-32] and physiologic and psychological stress, [33-39] alter immune function with the majority of evidence suggesting an adverse effect by suppression of natural killer (NK) cells,[40-43] and a decrease in the generalized immune response [44] .

Our study is in agreement with findings from those of Spiegel et al where the effectiveness of a similar non-

invasive cognitive-behavioral therapy showed improvements in survival between groups [45]. Their study showed that a support group intervention improved survival in patients with metastatic breast cancer. The intervention, which has some of the same components as the CCSP, focused on improving communication and sharing information, facing and mastering fears about death and dying, and controlling pain and other symptoms [45]. Receiving information about what to expect in relationship to specific procedures and treatment side effects is expected to increase the patients' sense of control, use of positive problem-solving activities, and ability to deal with the event by selecting better coping strategies. Also, learning how to recognize and avoid negative thinking, and use positive coping strategies should give the patient more control and increase their ability to cope.

Progressive muscle relaxation and imagery have been found to help patients to either escape problems or think of problems in alternative ways [46,47]. Several studies have shown that relaxation and imagery appear to reduce the sensory experience of pain, and have equivocal effects on affective measures. Cognitive behavioral training helps develop coping skills and lessens the pain, anxiety and depression which may exacerbate symptoms [48]. The efficacy of relaxation and psychological counseling is well established [48].

The CCSP might have been effective because of the combination of treatment strategies used which made the intervention more effective. Woods wrote that often cognitive-behavioral interventions demonstrate no positive effects because the treatment is not potent enough. [49]. To create a powerful treatment, it is logical to use a multi modal intervention such as the CCSP. Because the symptoms associated with treatment of breast cancer are multidimensional experiences, logic suggest using a multi modal strategy to successfully effect a change in these symptoms [48]. The CCSP has been shown to be effective in reducing multiple symptoms such as pain, and psychological distress, and improving the feeling of well-being of patients with breast cancer.

By reducing multiple symptoms, the CCSP may prevent the adverse effects that stressors like pain, anxiety and depression have on the immune system. On the other hand uncontrolled pain, anxiety, and depression can cause a decrease in NK cells and generalized suppression of the immune system in patients who are already immune compromised by the AT. This situation may be a major factor affecting a patients health status and survival. The mechanisms of action regarding cognitive-behavioral therapies and the attenuation of pain and other symptoms, however requires further elucidation [48].

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Table 1

Socio-demographics, mortality, breast cancer stage and chemotherapy type among Breast cancer patients undergoing ABMT and receiving CCSP

Attributes	CCSP@ (N=52) n(%)	Control(N=58) n(%)
Deaths	4(7.7)	12(20.7)*
Year of entry for ABMT 1995-1996 1996-1997 1997-1998	 15(28.8) 18(34.6) 19(36.5)	 20(34.5) 18(31.0) 20(34.5)
Age 22-40	11(21.2)	17(29.8)
41-50	26(50.0)	32(56.2)
51 and over	15(28.8)	8(14.0)
Race White	46(88.5)	48(82.8)
Employed	38(73.1)	36(62.1)
Married	47(90.4)	33(56.9)***
Education =< High School	8(15.4)	10(17.5)
Some College	10(19.2)	18(31.6)
College/Grad.degree	34(65.4)	29(50.9)
Occupation - Professionals	34(65.4)	32(55.2)
Income Less than 50K	10(19.2)	22(37.9)*
Cancer Stage Stage II	8(15.4)	13(22.4)
Stage III	32(61.5)	17(29.3)
Stage IV	12(23.4)	28(48.3)
Chemotherapy type I	22(42.3)	30(56.9)
II	30(57.7)	25(43.1)
Prior Coping Methods	21(40.4)	12(20.7)*
Prior Relaxation Methods	20(38.5)	18(31.0)
Mean Survival Period(days)(s.d.)	341.2(183.5)	233.3(166.0)

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* P <0.05 *** P<0.001

Table II

Association of intervention, year since follow-up , breast cancer stage, chemotherapy type, participant characteristics and mortality among ABMT breast cancer patients

Attributes	Deaths %	O.R. (95%CI)
Intervention(CCSP)@	4(7.7)	0.3(0.1-1.1)
Follow-up since ABMT		
2-3 years	11(31.4)	8.5(1.7-41.6)***
1-2 years	3(8.3)	1.7(0.3-10.7)
up to 1 year	2(5.1)	1.0
1-3 years	14(19.7)	4.5(1.0-21.1)*
Age 22-40 years	1(3.6)	0.2(0.2-1.3)
41-50 years	11(19.0)	1.0
51 years and over	4(17.4)	0.9(0.3-3.2)
Race - White	14(14.9)	1.2(0.2-6.0)
Employment Status - Employed	9(12.2)	0.6(0.2-1.7)
Marital Status - Married	14(17.5)	3.0(0.6-13.9)
Education =< High School	4(22.2)	2.8(0.7-11.1)
Some College	6(21.4)	2.6(0.8-9.1)
College/Grad.degree	6(9.5)	1.0
Occupation -- Professionals	5(7.6)	0.2(0.1-0.8)**
Income - Less than 50K	2(6.3)	0.3(0.1-1.4)
Cancer Stage Stage III	6(10.0)	1.0
Stage IV	9(31.0)	2.2(0.2-19.6)
Stage II	1(4.8)	9.0(1.0-77.5)**
Chemotherapy type I	15(27.3)	20.2(2.6-159.1)***
II	1(1.8)	1.0
Prior Coping Methods	2(6.1)	0.3(0.1-1.4)
Prior Relaxation Methods	4(10.5)	0.6(0.2-2.0)

@ Comprehensive Coping Strategy Program
* P=0.05 ** P <0.05 *** P<0.01

Table III

Adjusted Probability of Mortality Associated with CCSP@treatment among Breast Cancer Patients Undergoing ABMT

Attributes	Odds ratio (95%CI)
CCSP	0.11(0.01-1.00)*
Age 22-40 years	0.09(0.0-1.9)
41-50 years	1.0
51 years and over	0.80(0.1-7.7)
Race - White	0.063(0.1-7.1)
Employment Status - Employed	0.94(0.1-6.6)
Marital Status - Married	1.89(0.1-26.8)
Education =< High School	4.58(0.2-84.1)
Some College	3.10(0.2-40.9)
College/Grad.degree	1.0
Occupation – Professionals	0.01(0.0-1.5)
Income - Less than 50K	0.05(0.0-0.7)**
Cancer Stage Stage II	1.0
Stage III	5.7(0.2-165.9)
Stage IV	14.50(0.5-405-7)
Chemotherapy type I	38.8(1.3-1136.2)**
II	1.0
Prior Coping Methods	0.17(0.0-4.1)
Prior Relaxation Methods	2.87(0.2-38.1)
Follow-up since ABMT 1-3 years	0.16(0.0-3.9)

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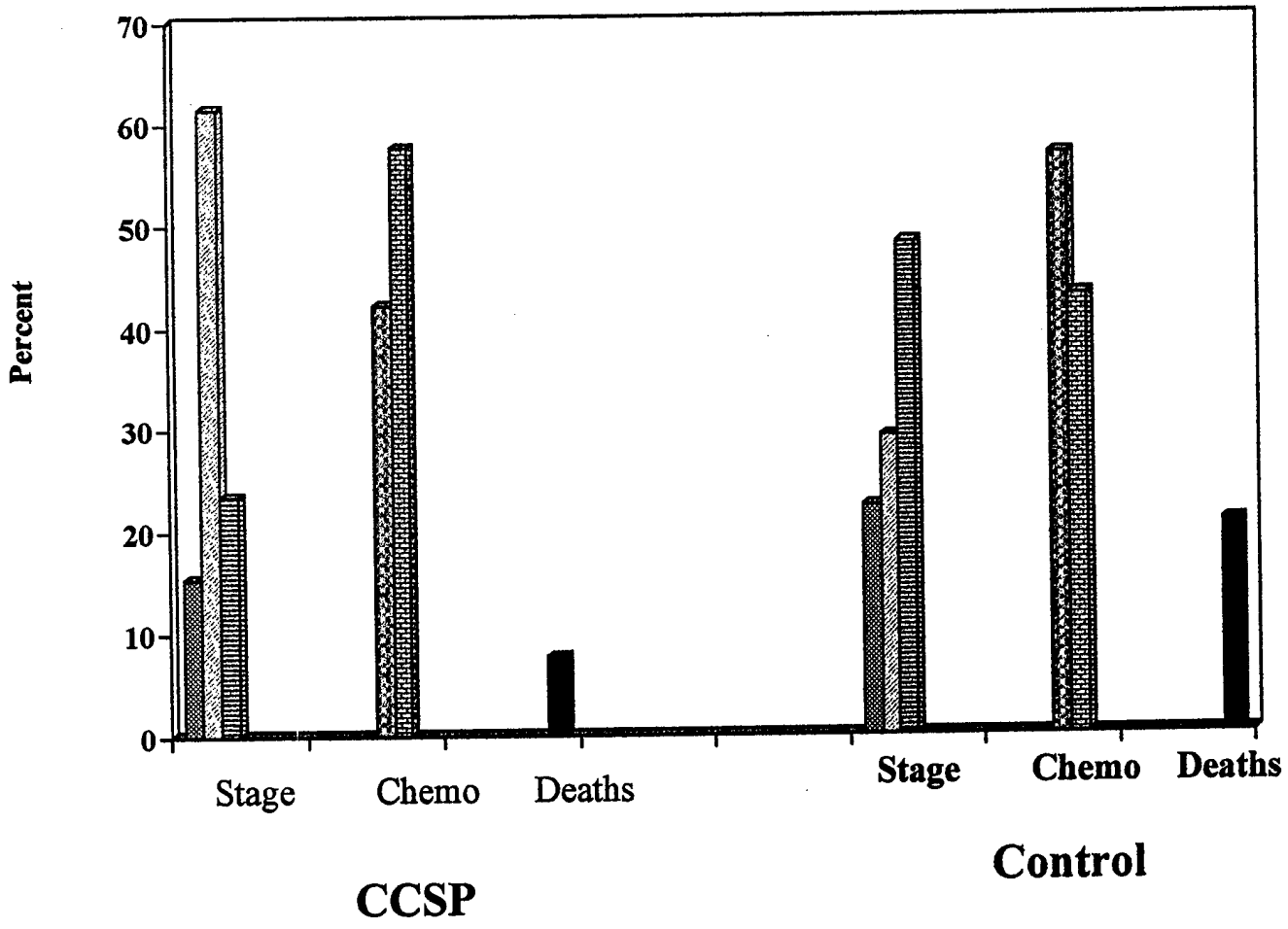
*P=0.05; ** P<0.05

Figure 1

Group Differences between Metastatic Stage, Type of Chemotherapy and Deaths between ABMT Breast Cancers patients receiving CCSP@ and their Controls



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Survival Analysis for SURVTIME # days alive/ to death at f_u

		Total	Number Events	Number Censored	Percent Censored
GROUP	control	58	12	46	79.31
GROUP	CCSP	52	4	48	92.31
Overall		110	16	94	85.45